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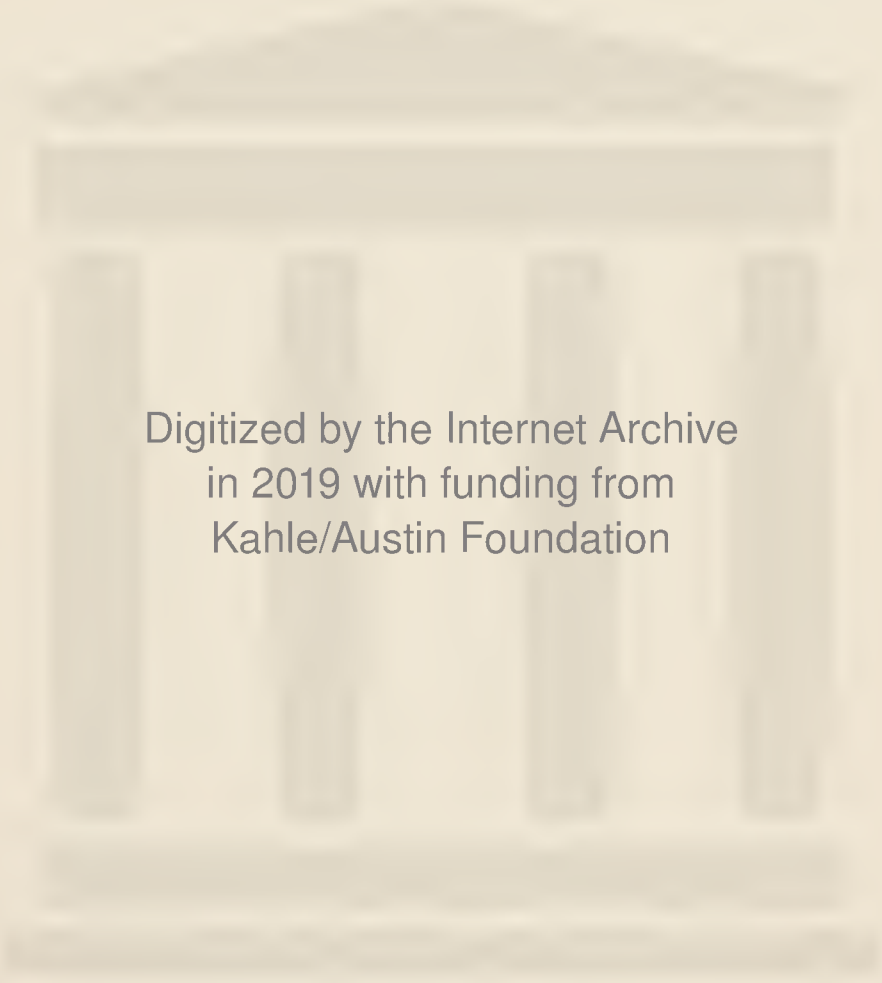

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Reflexes and Motor Integration:

Sherrington's Concept of Integrative Action

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Reflexes and Motor Integration: Sherrington's Concept of Integrative Action by Judith P. Swazey

Sir Charles Scott Sherrington, 1857–1952

Reflexes and Motor Integration: Sherrington's Concept of Integrative Action

Judith P. Swazey

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To Peter

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Monographs in the History of Science

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Foreword

Because of the dominant position still occupied by Charles Scott Sherrington (1857–1952) in the field of physiology — notably neurophysiology — several of his younger colleagues and associates (and others who felt themselves in his debt) have set down their own appraisals of his work and influence. Most recently, Ragnar Granit, Nobel laureate in medicine for 1967, took the measure of Sherrington's influence on modern neurophysiology in a sympathetic and perceptive study. Articles and books on Sherrington written by professional physiologists bring to the fore a problem fundamental to the writing of the history of the science of our own day: there are certain technical aspects of the work of a modern scientist which can be fully understood or appreciated only by fellow scientists. We are, therefore, profoundly in the debt of those of today's working scientists who have taken the time and demonstrated the interest necessary to provide historical commentary upon recent scientific developments. Yet the writing of the history of recent science, if maximally successful, will almost certainly require the efforts of the well-trained and perceptive historian, perhaps working together with professional scientists, or at least drawing heavily on their interpretive accounts of the recent developments within their disciplines.

Mrs. Swazey's study is a particularly fascinating illustration of the interplay between the historian's analysis and the scientist's presentations. And the subject, Sherrington himself, is a more than apt choice, for he was fascinated not only by scientific research but by the study of the history of science. He wrote a now-classic monograph on the sixteenth-century physician and scientist Jean Fernel; his celebrated book, *Man on his Nature,* abounds in historical insights; and he was, at the very end of his life, an active member of the Royal Society's committee on Isaac Newton.

Mrs. Swazey brings to her study of Sherrington the skills of an historian of biology. Drawing on the rich primary sources and documents, she has focussed her primary attention on the development of the concept of integrative action; the novelty of

her approach lies in new ability to assay Sherrington's earlier anatomical, histological, and physiological work in an effort to determine the role played by these earlier studies in his important physiological generalization. Sherrington's early training and his relationships with other members of the scientific community are also examined with respect to their importance in the development of Sherrington's thought and the growth of his technique as a neurophysiologist. Going beyond mere technical history, Mrs. Swazey has constantly endeavored to provide the historical perspective needed for the complete estimation of the life and work of one of the great figures in the history of physiology. To fulfill such an assignment is a major task for the historian of science (or scientist turned historian) who is concerned with the science of our own times. The complexity of this task points up both the dependence of historians on accounts written by scientists (often for other scientists) and the concurrent independence of method and judgment which the historians must exercise to go beyond such accounts into the background materials and the primary sources. The results of Mrs. Swazey's investigations demonstrate that a fine balance between dependence and independence, once achieved, establishes an appropriate framework for historical judgment.

This third volume in the Harvard Monographs in the History of Science, by its presentation of the life and scientific work of an almost contemporary scientist, emphasizes the broad range of the series.

Everett Mendelsohn

October 1968

Preface

In one of the most sustainedly productive careers in the annals of science, his writings covering a span of sixty-nine years, Sir Charles Scott Sherrington "almost singlehandedly crystallized the special field of neurophysiology." [1] Sherrington's classic investigations dealt primarily with reflex motor behavior in vertebrates, with the nature of muscle management at the spinal level.

The data, terms, and concepts which he introduced have become such a fundamental part of neurophysiology that it perhaps is not surprising their authorship is often forgotten. In my first physiology course I soon became familiar with terms such as proprioceptive, nociceptive, recruitment, fractionation, occlusion, myotatic, neurone pool, motoneurone, and synapse, and with concepts such as the final common path, the motor unit, the neurone threshold, the excitatory and inhibitory synapse, proprioception, reciprocal innervation, and the integrative action of the nervous system. When, as a graduate student in the history of biology, I learned that these core contributions to neurophysiology were largely the work of one man, Charles Scott Sherrington, the seeds of this study were sown.

As I began to read Sherrington's extensive writings two major goals took shape: first, to analyze the concept with which his name is linked most closely, "the integrative action of the nervous system," as that concept developed in his work from 1884–1906; secondly, to examine the significance of the integrative action concept for neurophysiology and, on a broader level, for the nature of biological thought. These two broad lines of inquiry in turn raised many questions to which biologists or historians of biology want answers. First, and perhaps most obviously, just what does the phrase "the integrative action of the nervous system" denote? A preliminary answer may be given from the pages of the Silliman Lectures which Sherrington delivered at Yale University in 1904 and published in 1906 as *The Integrative Action of the Nervous System.* Integrative action, he wrote, is the "action in virtue of which the nervous system unifies from separate organs an animal possessing soli-

darity, an individual . . . The due activity of the interconnexion resolves itself into the co-ordination of the parts of the animal mechanism by reflex action.[2]

The foregoing definition, in turn, raises the question of what was new about Sherrington's concept. An extensive body of experiments on reflex action were available when he began his researches, and Sherrington himself credited Pierre Flourens, a noted French investigator, with "formally" introducing the idea of nervous coordination into physiology during the 1820's. Precursors may be unearthed for virtually every discovery or concept in the history of science, for each advance in knowledge usually is a mixture of the old and the new. In this light it is meaningful to ask when and where the new outweighed the old in Sherrington's work. How did he arrive at the integrative action concept, and why does his work, embodied in that concept, mark a watershed in the history of neurophysiology?

Answers to these questions about the content, genesis and development, and significance of Sherrington's work have been sought from several sources. First, a study of the "personal equation" — the interests, events, and influences that helped to shape Sherrington's own life. Second, a survey of the relevant knowledge about reflex action and the functional anatomy of the spinal cord, gross and microscopic, at the time he began his researches. Third, a detailed analysis of the major lines of Sherrington's own researches: anatomical studies of spinal degenerations, the distribution of motor and sensory roots in the macaque monkey, sensory nerves in and from muscles, the motor cortex, decerebrate rigidity, reciprocal innervation, and the reflex patterns of the spinal animal.

Finally, I have looked at Sherrington's work in terms of two major trends which appear to characterize the history of biology.[3] First, the development of biology as we know it today has been accomplished by a process of "atomization," a reduction of our working knowledge of biological phenomena to smaller and smaller components. Secondly, particularly during the nineteenth and twentieth centuries, a series of general statements have emerged from the synthesis of various research fields, formulating uniform laws of biological processes. The develop-

ment and statement of the integrative action concept by Charles Sherrington, I believe, provides a fruitful example of one way in which these dual patterns of explanation in biology can operate.

The material in this study was originally prepared under a National Institutes of Health predoctoral fellowship from 1963 to 1966, and was presented to the Department of the History of Science, Harvard University, as my doctoral dissertation.

Shortly after I began work on my dissertation I learned that Professor Ragnar Granit, who studied under Sherrington in 1928 and from 1932 to 1933 and presently is Director of the Nobel Institute of Neurophysiology, Stockholm, was writing a book on Sherrington for the British Men of Science series published by Thomas Nelson and Sons. Professor Granit's book provides a detailed appraisal of Sherrington's major experimental and conceptual work in the decades after *The Integrative Action* was published, concentrating upon his researches at Oxford in the 1920's and tracing up to the present many of the issues which that work raised.

My own study, I hope, will serve as a useful complement to Professor Granit's, as well as to a work we have both found invaluable, Professor E. G. T. Liddell's *The Discovery of Reflexes.* The authors of a 1952 paper on "the early history of the reflex" aptly characterized the past century of neurophysiological researches with the following words: "Whatever the future, the age that is now ending has been the age of the reflex, and whether or not the experimentation and thinking it has occasioned have or will ever have validity in accounting for the dynamics of behavior, the concept of the reflex has been for better or worse the most significant development in neurophysiology during this period."[4] As I have learned, and have attempted to convey in the pages that follow, the methodological, experimental, and conceptual contributions of Charles Scott Sherrington in the period 1884–1906 were a decisive factor in shaping the "age of the reflex," and have left a lasting imprint upon neurophysiology.

J. P. S.

Acknowledgments

Apart from published materials by or concerning Sherrington, a major source of information about his life and work has been the papers of the late Dr. John F. Fulton, housed at Yale University's Historical and Medical Library. Dr. Fulton's close personal and professional association with Sherrington lasted thirty-one years, from the time Fulton went to Oxford as a Rhodes Scholar in 1921 until Sir Charles's death in 1952. During those years Dr. Fulton compiled an extensive collection of "Sherringtonia," including correspondence, memorabilia, and information on his life and work. The Fulton collection, especially his notes and diary entries, provides many fascinating new glimpses into Sherrington's character and the course of his life. But for purposes of historical analysis much of the material cannot be accepted at more than face value: as recollections by Sherrington and others of events which often occurred many years before their telling, and as Dr. Fulton's anecdotes and estimates of a close and admired friend.[5]

My study of Sherrington and the integrative action concept has been aided and enriched by the assistance of many people. I appreciate the time which several of Sherrington's former pupils, colleagues, and friends took to answer my inquiries about his work. Special thanks are due to: Mr. Thomas D. Briden and Mr. Wallace F. Morfey of Ipswich, England, for providing me with information about Sherrington's career at the Ipswich School; Mr. Carr E. R. Sherrington, who has so patiently answered my many queries about his father; Miss Madeline Stanton, Librarian of Historical Collections at Yale's Historical and Medical Library, who made Dr. Fulton's papers available to me and assisted my research in countless other ways; Mrs. Robert C. Moellering, Jr., for editorial assistance in the preparation of this manuscript.

The completion of this study owes much to the innumerable thoughtful suggestions and criticisms of Professor Everett Mendelsohn of Harvard University.

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Reflexes and Motor Integration:

Sherrington's Concept of Integrative Action

I

Sherrington: The Man and His Journey

The scientific journey has no end. It has only halting places — points at which the traveller can look round and survey.

— *Man on His Nature*

Sir Charles Scott Sherrington, the scientist whose *Integrative Action of the Nervous System* has been termed "the *Principia* of physiology" and the philosopher-poet who wrote *Man on His Nature* and *The Endeavour of Jean Fernel,* is a name familiar to many. But for most people, Sherrington the man is no more than a legend. "Even those who met him," observed a former pupil, may recall only that he was a "shy man with a small body and a preoccupied manner; a man oblivious to his own great stature and reputation." [1]

Toward the end of his life Sir Charles often said earnestly that he hoped no one would write his biography. He had high standards of accuracy and felt that a biographer can seldom if ever accurately portray the thoughts which guided another's life and work. "The mind," he believed, "made the man, and its achievements alone are worth recording." [2] But the writer of *Jean Fernel,* one feels, would agree that the development of a concept such as the integrative action of the nervous system may be better understood by going beyond the published work of its originator, toward a recognition of the influences and events that shaped the man and his ideas.

The bare record of Sherrington's career, noted Lord Adrian, "shows us a man who rose to scientific eminence by the accustomed route." [3] Born in London in 1857, his academic training progressed from the Ipswich School to medicine at London's St. Thomas's Hospital in 1876, Caius College, Cambridge, in 1879, the completion of his medical courses, and graduate studies and research in Cambridge and Europe from 1884 through 1887. He became Superintendent of the Brown Institution, an animal hospital in London, in 1891, Holt Professor of Physiology at Liverpool in 1895, and Wayneflete Professor at

Oxford in 1912. His numerous honors included the Presidency of the Royal Society of London from 1920 through 1925, the Knight Grand Cross of the British Empire in 1922, the Order of Merit in 1924, the Nobel Prize in Physiology and Medicine in 1932; at his death in 1952 he was an honorary fellow, member, or associate of over forty academies and had received honorary doctorates from twenty-two universities.[4]

Sherrington, a colleague observed, gave of himself and showed himself most to those who worked in his laboratory. The research student would first enter Sherrington's laboratory timidly, "with a picture of the author of *Integrative Action* as a man who must dwell in a sphere of his own making, difficult to attain or to travel in — a man necessarily aloof and out of common reach, 'academic,' coldly intellectual." A first impression might be that, physically, this scientific giant was short in stature, about 5 feet 6 inches tall, precise and neat in his movements, with lively, humorous grey eyes peering through rimless spectacles, though their owner was not severely near-sighted.[5]

He would soon come to know Sherrington as a many-sided man, a man of diverse intellectual interests, conversant on topics ranging from Gothic architecture, painting, rare books, poetry, philosophy, and the aesthetic movement of the 1880's, to the history of mechanical invention, Darwinism, and Canada. He would see Sherrington the scientist, questioning, doubting, testing the material before him until the answers were clear; the teacher, who quite sincerely expected that each student would teach him something, sometime; the lecturer, whose hesitancies, qualifications, and complexities, so often bewildering to listeners, were due to his demands for exactitude; the poet and lover of poetry, who at the age of seventy-three was reciting by heart long passages from Bridge's *The Testament of Beauty* as he prepared experiments.[6]

He would become aware that perhaps Sherrington's most dominant personality trait, emphasized by all who knew him, was his extreme modesty: a colleague once described him as "ridiculously unassuming." [7] With modesty were linked a mild disposition and an undogmatic manner, making him deferent to the opinions of others, receptive to criticisms of his own

work, and reluctant to engage in scientific controversy. Associates recognized a "dear me" or "that is most annoying" as strong expressions of vexation from Sir Charles.

Lastly, the student might realize that Sherrington was shy and secretive about certain aspects of his life, especially his poetry, which he could seldom be induced to mention, and his age, which he kept a closely guarded secret until after his ninetieth birthday. By now Sherrington had become to his student a very human figure, a man who found "perennial pleasure" in science because "it's always on the move forward — always young of itself, it helps to keep its followers young, at least in interest." [8]

IPSWICH, LONDON, EDINBURGH: 1857–1879

The origins of Sherrington's broad interests and his careers as scientist, philosopher, and poet may be traced to the atmosphere of his childhood years. The future "main architect of the physiology of the nervous system" was born on November 27, 1857, while his parents were visiting Islington, London. His father, James Norton Sherrington of Yarmouth, died while Charles was very young. Mrs. Sherrington remarried and Charles grew up at Edgehill House, Ipswich, the home of his stepfather, Dr. Caleb Rose, Jr. Edgehill House, a gathering place for artists and scholars, was a home "that was literally full of pictures — on chairs, on tables — for there was no room to hang them. There were endless collections — fossils, shells, coins, stones, minerals and the like — for it was the age of collections — but there were endless books too, on architecture, archeology, medicine, the classics, and painting." [9]

The other members of the Rose household were Charles's two younger brothers, William and George, and his stepbrother, Edward Rose, a future dramatist and drama critic for London's Sunday *Times*. William Sherrington, who became a barrister and active Mason, died in 1912 or 1918, while George, an athlete of some note and later a solicitor, died about 1944. Neither of Charles's brothers married.[10]

The Sherrington brothers attended the Ipswich Grammar School. When Charles entered the school in 1870 his studies, following the pattern of the times, included classics, languages, history, and literature. The numerous prizes and commendations which he earned in these courses foreshadowed his adult interest and proficiency in many nonscientific fields.[11] School days at Ipswich were rounded out by athletic activities such as soccer, bicycling, rowing, and swimming, which Sherrington always enjoyed.

The two greatest influences upon the young Sherrington were his mother and stepfather, but his interests were also shaped by two of his teachers. H. A. Holden, a noted classical scholar and headmaster of Ipswich, led him toward his deep knowledge and love of classics. From Thomas Ashe, an assistant master and poet, Sherrington derived his zeal for foreign travel and the fondness for poetry, literature, and books that became his "first and last love" toward the end of his life. Ashe aroused especially his admiration for Keats, the ideal whom Sherrington tried to emulate in his own verses.[12]

Sherrington's last year at Ipswich, 1875, seems to have been spent mostly in independent study, presumably preparing "special subjects" for his entrance into medicine.[13] That his proficiency in the traditional grammar school curricula was matched by a flair for science is indicated by the outcome of the year's work. Although it was unusual for a student to pass medical examinations prior to study at Cambridge or Edinburgh, Sherrington passed the Preliminary Examinations in General Education of the Royal College of Surgeons in June 1875 at the age of eighteen. In September 1876 he became a pupil at St. Thomas's Hospital, London.

In later years Sherrington recalled that his interest in medicine had been first aroused by reading a passage about M. F. X. Bichat, a noted eighteenth-century French anatomist and surgeon, in Carlyle's *French Revolution*. His decision to enter the medical profession, encouraged by Dr. Rose, was precipitated by a blow to the family's finances. "Because of a bank failure," his son related, "father had to give up thoughts of Cambridge and start a career; he chose medicine." Thus, with further encour-

agement from Dr. Samuel Wilks of London, Sherrington started his medical training at St. Thomas's.[14]

After a short time at St. Thomas's, Sherrington became a medical student at Edinburgh. In later years he spoke little of his days at Edinburgh, but his time there seems to have been unhappy and brief. In April 1878 he passed his Primary Examination for Membership in the Royal College of Surgeons, and by 1879 had returned to London, as witnessed by the appearance of his name on a cup as a member of St. Thomas's first fifteen at rugby for that year.[15]

CAMBRIDGE, LONDON, EUROPE: 1879–1887

In October 1879 Sherrington finally realized his desire to attend Cambridge. After three terms as a noncollegiate student, presumably with an improvement in the family finances, he was admitted to Gonville and Caius College on October 1, 1880. His progress at Cambridge is recorded in Caius College's *Biographical History* as follows:

B.A. 1884: M.B. 1885: M.A. 1887: M.D. 1893 Scholar, L.Day 1881 to Mich^{s} 1884. Nat. S. Tripos, 1881, P.I, cl.I, 1883, P.II, cl.1. Shuttleworth scholar, 1883. Lewes Student, 1884. Thurston Prize, 1887. Fellow, Mich^{s} 1887 to Mids^{r} 1893.[16]

The activities and interests nurtured at Edgehill House and Ipswich School flowered during Sherrington's Cambridge years, for his time was not devoted solely to the study of science and medicine recorded in the official records. Poetry, painting, and the study of printing, according to his son, were "his second, if not his first, interest," and time also was spent playing rugby and rowing for Caius. Vacations saw him journeying to Switzerland for winter sports, and wandering about Europe in search of medical knowledge, books, architecture, and improvement of his languages. He read Latin, French, German, Italian, Spanish, and Dutch.[17]

Training with Michael Foster. Sherrington always looked back with pleasure on his life at Caius where, having decided to sit for the natural sciences tripos, his work centered around

Michael Foster's physiology laboratory. A fledgling biologist in England of the 1880's could have chosen no better place than Cambridge for his research training, for in the words of Edward Sharpey-Schafer, Foster made "the bones of biological science, which had become very dry in Cambridge, live again." [18]

Foster, noted as teacher, writer, and organizer, had a large share in making practical laboratory work an essential part of the biological sciences in England. In 1869 he became Professor in Practical Physiology at the University of London, where he had received his M.D. in 1859, and succeeded Thomas Henry Huxley as Fullerian Professor of Physiology at the Royal Institution. Huxley, with Foster as his demonstrator, gave the first course in practical physiology in London in 1870. Foster brought to Cambridge Huxley's belief in the direct observation of natural phenomena and the value of research when he was appointed to the new post of Praelector of Physiology at Trinity College in 1870. He became Professor of Physiology at Cambridge in 1883, and was knighted in 1899. In 1878 Foster founded the *Journal of Physiology,* which was the first English journal devoted solely to the field. He also was largely responsible for establishing the Physiological Society in 1875 and the International Congress of Physiology in 1889. His talents as writer and organizer seemed to have surpassed his lecturing, for Sherrington recalled him as an "appalling lecturer" whose classes were seldom well attended.[19]

The changes in teaching that Foster brought to Cambridge chiefly affected physiology, which previously had been taught by lectures and the exhibition of specimens. Anatomy remained a purely topographical study, and pathology, for which no chair had as yet been established at Cambridge, was relegated to the museum and the postmortem room.[20] Foster soon organized practical classes in physiology, physiological chemistry, histology, biology, and chemistry, and wrote texts for them in collaboration with men such as John Burdon-Sanderson, Lauder Brunton, E. Klein, F. M. Balfour, and John Newport Langley.

Foster exemplifies a new type of scientist who emerged in the late nineteenth century. His major contribution to physiology lay not in creative researches but in a great ability to guide and

inspire students that resulted in the establishment of a highly productive and enduring research laboratory. A flood of "Papers from the Cambridge Physiological Laboratory" issued from Foster's active young researchers, such men as John Newport Langley, F. M. Balfour, Newell Martin, Sheriden Lea, S. H. Vine, W. H. Gaskell, Milner Marshall, and James Ward.

Shortly before his death Sherrington recorded his memories of the atmosphere at Cambridge during this biological renaissance, and of the men who influenced the course of his studies.

> I sat for the Natural Science Tripos. Things were stirring in the Medical School. Langdon-Brown has happily referred to Michael Foster, George Humphrey, and George Paget as the 'Great Triumverate.' But for me, an even more appealing triumverate, in that then small and ramshackle haunt of physiology, were Gaskell, Langley, and Lea, assistants to Foster . . . The Physiology School was small in numbers, but its camaraderie was something unforgettable. After taking an arts degree [1884] — I stayed up doing a research under Langley.[21]

His recollection of the day he took a "clinician of European repute" through the laboratories encapsulates the research tradition inspired by Foster. After watching Langley experimenting on salivation in the cat and Gaskell studying the excised tortoise heart, the clinician expressed his admiration for the work he had seen.

> But he then added that he was surprised and mystified by the problems chosen: such earnestness and care devoted to subjects quite remote from Medicine! . . . All I could say did nothing to shake his conviction that all this devoted laboratory work was as regards Medicine sadly beside the mark. The coming years however were not slow to answer this criticism. Langley was discovering what to this day is the fullest picture of secretion as a cell-process. Gaskell was laying the foundation of . . . 'Modern Cardiology.' [22]

In addition to his work in the physiology laboratory, Sherrington served as student-demonstrator in anatomy to Sir George Humphrey in 1883, and as demonstrator in histology at St. Thomas's for the winter session of 1883–84. Sir George, who also supervised some work of Sherrington's at Addenbrooke's Hospital, remembered that he had been "much impressed by [Sherrington's] ability and assiduity. He did his work well, and the

students were much attached to him. His genial friendly qualities made him a general favorite and a most agreeable colleague." [23]

Beginning research. The first of Sherrington's more than 300 publications appeared in January 1884, near the end of his undergraduate days at Caius. The paper, with J. N. Langley as senior author, stemmed from one of the most dramatic incidents in the history of physiology. The Seventh International Medical Congress met at London in 1881. With Michael Foster as chairman of the physiology section, two leaders of neurophysiology — F. L. Goltz of Strasbourg and David Ferrier of England — clashed over the question of localization of motor control in the cerebral cortex.[24]

The nature and localization of brain functions was one of the most intensively debated problems in nineteenth-century physiology. Researchers were divided into two general camps, especially as concerned the "psychic" functions of the cerebrum. In the first half of the nineteenth century these camps were led by the German physicians Franz Joseph Gall (1758–1828) and J. C. Spurzheim (1776–1832), who held that specific functions have highly specific loci within major subdivisions of the brain, and by the French physiologist Pierre Flourens (1794–1867), who advocated the more widely accepted view that each major subdivision exerts a unitary function.[25]

The first major challenge to Flourens' account of the brain as a fairly simple organ came in 1861, when the French surgeon Paul Broca announced localization of a speech center in the left hemisphere. Within a decade Broca's clinically derived principle of functional localization gained support from experimental physiologists' localization of motor and sensory centers. In 1870 Gustav Fritsch and Eduard Hitzig electrically stimulated the dog's cortex, thus overthrowing the belief that the cortex was inexcitable, and demonstrated localized areas controlling five separate groups of muscles. David Ferrier in 1873 found that when specific areas of the excitable cortex were surgically removed, the member that had previously responded to electrical stimulation suffered motor paresis.

In arguing for specific localization of function at the 1881 Congress, Ferrier demonstrated two monkeys, one of which was completely deaf ten weeks after lesions of both superior temporal convolutions were experimentally induced. The second monkey, a hemiplegic, evoked from the French neurologist and pioneer psychiatrist Charcot the memorable remark, "C'est un malade." Goltz, in turn, maintained Flourens' view that the cerebrum does not exhibit specific functional localization, for the dogs from which he had made cortical excisions showed no evident paralysis or other disturbances.

In an attempt to resolve the deadlock and calm the tempers raised by the debate, a committee composed of W. R. Gowers, E. Klein, E. A. Schäfer, and Langley was appointed to study and prepare reports on neural material from one of Ferrier's monkeys and from Goltz's dog.[26] John Langley received the right half of the medulla and spinal cord of Goltz's dog. He became rather weary of the lengthy and laborious histological study, and in the winter of 1881–82 he asked his student, Charles Sherrington, to assist him with the task. The offer was accepted, and Sherrington was launched upon his first piece of scientific research. He apparently did not hear Goltz's and Ferrier's debate, as he is not listed as a member or student member of the Congress, but Fulton noted that Sherrington's interest in neurophysiology had been aroused before he went to Cambridge by his reading about Ferrier's researches.[27]

Studies in Europe. Sherrington's research with Langley by no means had settled him upon a career in neurophysiology, for early in the 1880's he had decided to become a pathologist.[28] In pursuit of this goal, as well as of his general interests in medicine and physiology, his work during 1884–1887 became a busy blend of clinical, laboratory, and field studies in England and Europe. Sherrington's memories of these years provide fascinating glimpses of his scientific training and of the many leaders of late nineteenth-century biological sciences under whom he worked.

Part of 1884 was spent at St. Thomas's, where Sherrington continued his clinical studies. The atmosphere of a great city

hospital clearly made an indelible impression upon his mind.

> I imagine that in the training for no other profession does so great a shift of contacts happen so abruptly as for the student in Medicine — or at least did so seventy years ago. The plunge from laboratory life in Cambridge to out-patient work among the poor of a great hospital in London is an experience startling and ineffaceable — an excursion into a strange world. St. Thomas's Hospital dates back to the twelfth century, and is more than coeval with 'Bart's.' Its site was for centuries in St. Thomas's Street, the street in which Keats wrote his famous sonnet on Chapman's Homer . . . In 1870 Queen Victoria opened its new buildings, facing the Houses of Parliament across the tidal Thames . . . Its students are an admixture of London, Oxford, and Cambridge. It serves a population which stretches from Bermondsey to Brixton Church, perhaps a million souls. In my student times its 'parish' extended across the river as well — what was then called Regency Street, Millbank, was then the very climax of its poverty.[29]

Clinical work was interrupted in 1884 when Sherrington won the George Henry Lewes Studentship for Physiological Research, enabling him to spend the remainder of that year and part of 1885 studying under Goltz at Strasbourg. He had planned first, at Foster's suggestion, to work at Bonn under Professor Eduard Pflüger (1829–1910), who was averse to having foreign students in his laboratory but finally accepted Sherrington on Foster's recommendation. Sherrington's first meeting with the eminent German physiologist, whose classic "laws" of reflex action would be undermined in a few years by the young Englishman's researches, was a memorable one. After greeting his new student, Pflüger took him by the arm and said, "und nun wir wollen einer Entdeckung machen" ("and now we will make a discovery") — whereupon they went upstairs to the laboratory and proceeded to discover a nerve in the gall bladder.[30]

Sherrington stayed with Pflüger only one or two months, working upon what he later described as a "fruitless" piece of research concerning the gases dissolved in bile. He then traveled to Strasbourg to work in Goltz's laboratory for a year. One of his most vivid memories of that year was the experience of seeing Alsace becoming rapidly Germanized. He lived in a lodging house run by the widow of a German parson and years later re-

called his surprise at finding that most of his fellow lodgers were young Germans serving in the army. It was all very astonishing to the young Englishman, for military service then was not considered part of an English gentleman's training.[31]

The age of the teaching laboratory was in full flower in Germany during the 1880's, stemming from the establishment of Jan Purkinje's physiology laboratory at Breslau in 1824 and Justus Liebig's chemistry laboratory at Giessen in 1825. With the teaching laboratory came a new pattern of scientific research, each "school" tending to develop its own approach to scientific studies under the aegis of its "master." [32] Goltz's institute clearly was devoted to research. No practical classes were held and every condition in the laboratory seemed designed to foster investigation rather than instruction. The master, who lived with his wife in rooms above the laboratory, came downstairs in bedroom slippers at eight each morning to deliver an hour's formal lecture and was seldom seen by his students for the remainder of the day.

As was common practice, Sherrington began his research apprenticeship with problems supplied by Goltz. Much of his time was devoted to microscopy and to the study of secondary and tertiary nerve fiber and tract degenerations, affording him further valuable training in experimental methods. His deepening interest in problems of central nervous system structure and function is evidenced by his first independent paper,[33] published from the laboratory in 1885.

Sherrington profited greatly from his work, feeling that Goltz had taught him "that in all things only the best is good enough." Goltz in turn had a high regard for his English pupil, commenting some ten years later that he esteemed Sherrington as both a successful observer and an extremely skilled experimenter.[34] That Sherrington and Goltz's relationship had its dissonant moments, however, is suggested by an anecdote which Fulton recorded in two differing versions. According to an unpublished version, Sherrington presented Goltz with two monkeys when leaving for a holiday, saying "Herr Geheimrath, perhaps if I present you with these two animals you will use them to discover the truth of Ferrier's contentions." When Fulton pub-

lished the anecdote he wrote that the monkeys were presented as a parting gift and that Goltz, misconstruing Sherrington's motives, felt that the "audacious young Englishman" was trying to alter the views he had expressed at the 1881 Congress.[35]

After his training with Goltz, and having qualified as M.R.C.S. Eng. (Member of the Royal College of Surgeons) and M.B. Cantab. (Medicinae Baccalaureus, the first degree in medicine), Sherrington took advantage of an opportunity to pursue his interest in pathology. In the summer of 1885, he, Charles Smart Roy, and Dr. J. Graham Brown were appointed by the Association for Research in Medicine and the Royal Society to investigate an outbreak of Asiatic cholera in Spain.[36]

The trio's adventures began with their arrival in Madrid, which they found half empty. The epidemic was ending there, but soon broke out in the small nearby town of Aranjuez, which was promptly cordoned off. When the young researchers finally obtained permission to enter the town, their sanitary precautions were ridiculed by the Spanish authorities and their work was hampered because the priests at first forbade them to perform autopsies. One old priest, convinced that cholera was due to a gall stone, anxiously awaited examination of the gall bladder at each necropsy. He was, however, doomed to disappointment, for the twenty-five autopsies performed by the Englishmen clearly showed the causative bacteria in the feces and nasal mucous membrane of the fatal cases.[37]

The following year Sherrington set out alone to investigate an outbreak of cholera in Italy, spending two summer months in Venetia and Puglia. Having run out of money in Venice, he earned his living for a time practicing medicine and, taking advantage as always of the chance to enrich his other interests, acquired his life-long taste for Italian incunabula. His knowledge of Italy and its culture was to make a great impression years later upon one of his students. After dining with Sherrington one night John Fulton wrote that Sherrington "seems to know every picture in Italy, and the exact year in which it was painted. He becomes so interested in what he is talking about that he forgets to serve anyone; it's delicious to see him." [38]

From Italy the prospective pathologist journeyed to Rudolph

Virchow's laboratory in Berlin and began to cut tissue sections from his cholera specimens. Prior to his arrival Sherrington had not realized that the great Virchow had passed his scientific prime and was devoting most of his time to politics as an opponent of Bismarck. Virchow lectured to his students on Saturdays, generally arriving late and "leaving after about twenty minutes of an ill-digested and ill-prepared lecture," saying that he had an important engagement at the Reichstag.[39]

Groups of Virchow's students were often taken to the Reichstag to hear Bismarck speak. Through such visits Sherrington came to feel the impotence of opposition to the powerful militarist, whose appearance reminded him of a "cuckoo set high in a cuckoo clock. The door opened. Bismarck appeared, read his speech without looking up and on conclusion folded his papers and disappeared, not even troubling to hear the comments on his speech." [40]

Sherrington stayed with Virchow for only two months, feeling dissatisfied with the facilities and opportunities for study in the laboratory. His departure for a year's work in Robert Koch's Berlin laboratory was made possible by Virchow. Pausing one day to examine some of Sherrington's cholera tissue, Virchow called him into his office, said very briefly, "with sections like that you ought to be in Koch's laboratory," and promptly wrote a letter of recommendation.[41]

After taking the laboratory's required six-week course in bacteriological technique, training which Sherrington valued greatly, he continued his pathology researches. Koch appeared each Saturday forenoon to examine the work of the seven or eight students in his laboratory. On one such occasion Sherrington was studying microscopically a stained kidney section from a mouse killed by anthrax. The kidney's blood vessels were so filled with bacilli that he thought they almost looked infected. As Koch was examining the preparation Sherrington asked, " 'Herr Geheimrath, how does it kill?' He replied, 'Why, its vessels are plugged with bacilli!' I was surprised — 'A mechanical death?' The reply came 'Gewiss!' There was I fancy at that date very little chemistry in his pathology." [42]

While in Berlin Sherrington became acquainted with many

other great scientific figures of the day; he visited N. Zuntz's respiratory physiology laboratory, and he heard the tenets and results of reductionist physiology in the lectures of Hermann von Helmholtz and Emil Du Bois Reymond. Helmholtz he found to be a "shockingly bad lecturer" and a poor arithmetician, Du Bois Reymond an excellent speaker though somewhat spectacular and melodramatic. He also attended Wilhelm Waldeyer's course in histology, and never forgot the day when Waldeyer, pausing to observe a nerve-cell preparation, commented dryly, "Das Denk-Organ" ("the organ of thought"). Recounting the incident some forty years later Sherrington, who held quite different views on the ability of physiology to account for "mental" events, recalled his astonishment at the comment. Waldeyer's remark, he felt, "was mechanism in its crudest form." [43]

LONDON: 1887–1895

When Koch, at the end of Sherrington's stay with him in 1886–87, learned that his pupil's plans were unsettled, he advised that "for you, an Englishman, India is the place. Things are waiting there for investigation." Attractive as the proposal may have sounded to someone with Sherrington's zest for travel, he returned to England.[44] In the summer of 1887 he was elected a Fellow of Caius College and lecturer in systematic physiology at St. Thomas's.

That same year the young lecturer acquired one of his most helpful and devoted assistants, George Cox, who remained with Sherrington throughout his years of research. Later, as senior laboratory assistant at Oxford, Cox ruled the laboratory, its pupils, and often its master with a sure hand, and was known in places such as the Institut Pasteur as "Dr. Cox." Just before his own death Sherrington fondly recalled his long association with Cox and recorded a favorite laboratory anecdote.

> [George] was from a Church (elementary) school in Lambeth. His schoolmaster taught him . . . algebra after school hours; George profited in that and other ways . . . [He] picked up my laboratory work as though born to it. He became first rate at operative tech-

nique . . . He was fond of animals and became an expert in understanding and managing anthropoid apes, of which I had to use a number. We kept them in a large well-lighted room and such as were tamed we allowed freedom, and they mixed well with the other inmates — cats, dogs, rabbits, and guinea pigs . . . It once happened that George and I, after paying our usual visit to their room, and, on leaving, locking and taking the key with us, asked ourselves what the animals did after we were gone. Tip-toeing back, I put my eye to the keyhole, to look through. The hole seemed obstructed. I could make out nothing. Then suddenly I perceived that what blocked it was another eye much like my own . . . The chimpanzee had had the same thought as I and she had been there first. Female curiosity! [45]

Early in 1888 Sherrington became engaged to Ethel Wright of Preston Manor, England. Marriage became financially possible three years later, when the thirty-four-year-old lecturer was appointed Physician-Superintendent of the University of London's Brown Institution.[46] The Brown appointment was made on March 10, 1891, and on August 27 the couple was married by the Dean of Caius at Preston St. Mary. After a honeymoon abroad the Sherringtons settled into their London home at 27 St. George's Square, where they lived until they moved to Liverpool in 1895. Their only child, Carr E. R. Sherrington, was born in 1898.[47]

The London years were happy and active ones. Although Sherrington's rugby days had ended, weekends often were spent enjoying bicycling, tennis, sculling, and golf. Trials with silk parachutes from the tower adjoining the main building of St. Thomas's were a featured event on Sunday mornings. Ties with the Ipswich days were maintained through many evenings spent at the Hampstead home of Sherrington's stepbrother, Edward Rose. Both the Sherringtons enjoyed the literary circle, including George Bernard Shaw and Anthony Hope, and the many noted painters and engravers who gathered at Rose's home. The couple also enjoyed many trips abroad, for Physiological Congresses, winter sports, and summer bicycling tours. Summer trips often included visits to Paris, for Sherrington loved its Left Bank where he had once lived and worked.[48]

The nature of Sherrington's duties at the Brown Institution,

combined with his native abilities, enabled him to produce a prodigious amount and variety of researches during his four years as Physician-Superintendent. The principal duties of the Physician-Superintendent were to give free public lectures yearly on some aspect of his work and to do research. An animal hospital such as the Brown Institution provided an ample supply of animals for experimentation, and a survey of the papers published by Sherrington from 1891 to 1895 shows that he took full advantage of this opportunity.

At some point after his return from Berlin in 1887 Sherrington had decided to commit himself principally to neurophysiological rather than pathology researches. He continued, however, to explore problems in pathology and general physiology, publishing papers on subjects such as "The regulation of the blood supply of the brain," "Varieties of leucocytes," "The escape of bacteria with the secretions," and "A note on Cheyne-Stokes breathing in the frog." A noteworthy event during these non-neurophysiological studies occurred on October 15, 1894, when Sherrington became the first man in England to administer antidiphtheritic serum for therapeutic purposes. The story of this event is best told in Sherrington's own words. A friend with whom he experimented at St. Thomas's, Dr. Armand Ruffer, often made trips to Paris and brought back news of work at the Institut Pasteur.

> Returning from one of these visits he spoke of the treatment of diphtheria which was being tried out there. Injection of the serum of an immunized horse. He would like us to try it. I had a spare stall in the stable at my Veterinary Hospital, and we got a horse and began inoculating it with gradually increasing doses of diphtheria cultures. We had been at this a week or two, and had a serum at least partially effective in guinea-pigs. We were badly in the dark about dosage. Then oddly enough, one Saturday about seven in the evening, came a telegram from my brother-in-law in Sussex. 'George has diphtheria.' George, a boy of eight, was the only child. The house, an old Georgian house, was some three miles out of Lewes, set back in a combe under a chalk down. There was no train that night. I did not at first give thought to the horse, and when I did, regretfully supposed it could not yet be ripe for use. However, I took a cab to find Ruffer — no telephone or taxi in those days. Ruffer was dining out, I pursued him and got a word with him. He said,

'By all means, you can use the horse, but it is not yet ripe for trial!' Then by lantern light at the Brown Institution I bled the horse into a great four-litre flask duly sterilized and then plugged. I left it in ice to settle. Then after sterilizing smaller flasks and pipettes, drove home, to return at midnight and decant the serum, and sterilize needle-syringes. By Sunday's early train I reached Lewes. Dr. Fawssett of Lewes was waiting at the railway station in a dog-cart. I joined him, carrying my awkward package of flasks and such-like. He said nothing as I packed them into the dog-cart, but, when I climbed up beside him, he looked at me. 'You can do what you like with the boy, he will not be alive at tea-time.' We drove out to the old house. Tragedy seemed to shroud it. The boy was breathing with difficulty. He did not know me. The doctor helped with injecting the serum. The syringes were small and we emptied them time and again. The doctor left. Early in the afternoon the boy was clearly better. At three o'clock I sent a messenger to the doctor. Thenceforward progress was uninterrupted. On the Tuesday I returned to London and sought out Ruffer. His reaction was that we must tell Lister. The great surgeon had visitors, some Continental surgeons, to dinner. 'You must tell my guests', he said, and he insisted. Unlike as he and Pasteur were in some ways, they both as part of their inspiration had an unshakeable confidence in the immense future before medicine.[49]

While Sherrington's interest in general physiology and pathology never waned, it was soon overshadowed by the start of his major contributions to knowledge of vertebrate motor behavior, begun during his work at the Brown Institution. In a letter to Dr. Henry Head on November 23, 1918, he credited Walter Gaskell with focusing his attention upon the seemingly endless problems of deciphering the spinal cord's functions.

[Gaskell] was *always* an inspiration to me and to any work I was able to try. Such inspiration is often subtle and part of its success springs, I imagine, from its subtlety . . . My own work began by chance at the wrong end — the cortex — pyramidal degenerations, etc. It was certainly through Gaskell that I very soon felt that. One could not talk with him long without realizing that the cord offered a better point of attack physiologically . . . Later, too, when his own chief interest had passed to the origin of vertebrates, he was still always a bulwark to me about inhibition and voluntary muscles . . . That gift of sympathetic attention, and unselfish switching off from his own problem to a pupil's, was characteristic of his nature . . . In a hundred ways I owe him help and inspiration.[50]

Reflexes and Motor Integration

The first decade of Sherrington's researches on the spinal cord was occupied largely with establishing anatomical facts upon which to rest functional studies. Out of this work came his 1892 monograph of 150 pages on the peripheral distribution of the posterior root fibers of spinal nerves (following which he was elected a Fellow of the Royal Society in 1893), and his 1894 papers on the existence of sensory nerves in muscles and the nature of the sensory innervation of limbs. During the Brown years he also began his famous memoirs on reciprocal innervation, analyzing muscle management at the spinal level.

His researches into cortex-pyramidal degenerations led to one of the few occasions on which Sherrington, noted for his discretion and retiring ways, became publicly embroiled in controversy. The debate, with Sir Victor Horsley, was aired thoroughly in *Lancet* during February 1894.[51] Its content and effect upon one area of Sherrington's researches have been neatly summarized by John Fulton.

> Sir Charles had long been interested in the pyramidal tract owing to his early work on Goltz's dog. At the Brown Institution he found it possible to study the effects of isolated lesions of the arm and leg areas of monkeys and to follow by the Marchi technique the degenerations which resulted from such lesions. When he learned from Boyce that a Dr. Mellus of Berlin who had been in Horsley's laboratory in University College had undertaken similar work, he wrote a letter to the *Lancet* and put the matter in the clear. Horsley replied in an unpleasant manner, implying that Sherrington had held back information. In a second letter . . . Sir Charles was righteously indignant, and Horsley declared that Sherrington had declined to accept arbitration of the matter by a neutral committee. Thereafter all was silence, but Sir Charles was evidently so much upset by the episode that save for brief mention in notes published in 1901, 1902, and 1903 and a passing reference in his Silliman Lecture he withheld publication of his studies on the primate motor area and the degenerations resulting from isolated lesions until 1917, after Horsley had had a fatal sunstroke in Mesopotamia.[52]

LIVERPOOL: 1895–1912

The London years came to a close in 1895 when Sherrington accepted an appointment as Holt Professor of Physiology at Liverpool, after having unsuccessfully competed for the Wayne-

flete Chair of Physiology at Oxford. His predecessors in the Holt Professorship had been Richard Caton, less known than he should be for his pioneer contributions to the electrophysiology of the brain, and Francis Gotch, who moved on to Oxford where he again would be succeeded by Sherrington in 1912.

The Sherringtons' eighteen years at Liverpool were apparently the happiest of their lives, for the later Oxford period would be marred by the events of World War I. In and away from the laboratory Sherrington's activities were varied. Social events centered around the Philharmonic Concerts and the Repertory Company at Liverpool and the Richter Concerts at Manchester; sports included golfing at Hoylake, sculling on the Dee, and walking and bicycling trips.[53]

In their home at 16 Grove Park, Mrs. Sherrington, a skilled linguist and, like her husband, a lover of literature, architecture, music, and travel, was kept busy entertaining, helping Sherrington with his books, and looking after his papers. As their son tells us, the task of looking after his father's papers was no mean feat, for his study was "a welter of correspondence, pamphlets and books, that made the household task of dusting impossible. In contrast [to the care with which Sherrington preserved any letter he valued], any envelope brought by the postman which was considered to contain any income tax demand or a bill was promptly consigned to the wastepaper basket! Thus a family duty was to study their grim contents — that was my mother's daily task." [54]

No month went by at 16 Grove Park without a stream of visitors, including many from Canada and America. Sherrington must have been especially pleased with his Canadian guests, for since the days of his visits to Ontario, Canada "had stolen [his] heart." He came near, in fact, to moving to Canada in 1908. "There came a day when, having received an offer of a professorship at Toronto, after considerable cogitation [Sherrington] accepted and duly posted the acceptance on a Friday night. Second thoughts by the Sunday morning determined him to stay at Liverpool — he spent most of that Sunday at the General Post Office recovering the letter which was awaiting the next sailing to Canada." [55]

A second offer to emigrate to North America came in 1909, with a similar sequence of events. The offer, to go to Columbia University for twenty-five years, was duly pondered and then a cable of acceptance was written. Because it began to rain as Sherrington went out to mail the cable, he decided to wait until morning. When he awakened he had changed his mind and decided not to accept! [56]

Sherrington took an active part in university affairs and became a prominent figure in British scientific circles while at Liverpool. From 1889 through 1905 he was Honorary Secretary of the Physiological Society, succeeding Gerald Yeo. Concurrently, he was a general secretary of the International Physiological Congresses from 1892 through 1907, revealing his talents for organization and administration in the seven triennial congresses held during his tenure.[57]

His roles in academic affairs included organizing Liverpool's Thompson-Yates Laboratories of physiology and pathology in 1898, assisting in beginning new departments of psycho-physiology and veterinary medicine, and introducing a course and manual on school hygiene. He also began services for the government that would occupy much of his time during the First World War. From 1902 through 1906 he helped to conduct special investigations for the British Medical Association and government departments on the effects of chloroform. His service as a member of the Board of Sight-Tests Committee in 1910 and on the Home Office Committee on Lighting of Factories and Workshops in 1913 reflects his interest in problems of industrial fatigue.

All of his varied personal and professional "extracurricular" activities clearly were subsidiary to the eighteen years of virtually uninterrupted research at Liverpool. Testimonials from some of his colleagues in 1895, the year he was appointed Holt Professor, indicate the recognition that his work already had attained.[59] David Ferrier, whose researches had drawn Sherrington's attention in the 1870's, commented that his investigations "have assuredly gained for him the reputation of being one of the ablest and most philosophic investigators." Michael Foster, so able to recognize and nurture scientific ability, wrote, "the

work which Sherrington has already done shows that, as an enquirer, he possesses very marked originality of conception, combined with great patient exactitude in observation, and a very wide and accurate knowledge. These qualities are obvious in all his work, but perhaps especially so in his recent researches on the Afferent Factors in Muscular Movements." And Walter H. Gaskell, watching his former student reap the benefits of his advice to concentrate upon spinal cord physiology, wrote:

In my opinion, the work which Dr. Sherrington has done is of the very best type of English work: it is full of originality, bold in its conception, far reaching in its results, and he has shrunk from no amount of labour in order to ensure accuracy, even to the smallest detail. I look forward with the greatest confidence to his future work, for I know that whatever post he fills, he will never cease from the pursuit of scientific investigation. Such a man of necessity imparts his own enthusiasm to those around him.

The extent and variety of Sherrington's researches at Liverpool fully lived up to and perhaps surpassed the expectations of his supporters. So varied, indeed, was his work that one of his young research students gained a most misleading first impression of his abilities. When Harvey Cushing, the future American neurosurgeon, arrived at Liverpool in 1901 he wrote in his diary for July 21:

My first week has been consumed in the attempt to determine a line of work — Sherrington having no special suggestions — in finding out that an English laboratory may be in worse shape than an Italian one, and in watching two or three very interesting experiments.

The People. Sherrington is a great surprise. He is young, almost boyish if 36 (?) (actually 43,) nearsighted, wearing when he had not lost them a pair of gold spectacles. He operates well for a 'physiolog' but it seems to me much too much. I do not see how he can carry with any accuracy the great amount of experimental material he has under way. As far as I can see, the reason why he is so much quoted is not that he had done especially big things, but that his predecessors have done them all so poorly before.

The whole thing referrable to experimental neurology much to my surprise is still in a most crude condition. The problems offered are immense. Sherrington goes at them too fast. Few notes are taken during the observations, which is bad. Sherrington says himself he has a bad memory — putters around his laboratory till after 7 in

the evening trying to catch up on things, and then is used up and doesn't begin till ten or eleven the next day.[60]

Sherrington's research techniques and "great amount of research material" during his first twelve years at Liverpool will be our concern in the chapters that follow. A high point of those years came in 1904 when he journeyed to America as Yale University's second Silliman Lecturer. The lectures' publication in 1906 as *The Integrative Action of the Nervous System* left little room for doubt that the once prospective pathologist had become the leading analyst of reflex motor behavior.

OXFORD: 1913–1935

Sherrington continued his active life as researcher, teacher, writer, and prominent member of the international scientific community in the years after *The Integrative Action*. In 1913, thanks in large measure to the efforts of William Osler, he was called to the Wayneflete Chair of Physiology and a fellowship at Magdalen College, Oxford.[61]

The Sherringtons knew the Oxford area well, having spent many summer vacations there; Sherrington, indeed, knew each college and quadrangle so intimately that he could recite every detail of their architecture. The Sherringtons' first contact with Magdalen had been in 1896 or 1897, and judging from an episode recorded by Fulton it must have left them with mixed feelings concerning the atmosphere of their future college. They stayed with Sir Herbert and Lady Warren at Magdalen while attending a Physiological Society meeting at Oxford. The Society met on Saturday, and it was the custom to have a picnic up the River Cherwell on Sunday. When the Sherringtons told the Warrens that they were expected to go picnicking a look of horror came over their host's face, and he said gravely, "I suppose you will have to wear a sports frock — I will have a cab ready to meet you at the door." A cab was duly brought to the side door of Magdalen lodge and, to complete the picture, Sir Herbert's butler pulled down the shades inside the cab so the casually attired Sherringtons could not be seen as they drove out of the College on a Sunday morning.[62]

When he arrived at Oxford Sherrington found a flourishing department with ninety students. His teaching duties and research program, however, were soon curtailed by the war. When the school session opened in October 1914, he was left with seven students, and by 1916–17 his quarters had been reduced to two small rooms where he worked with only one pupil. His pupil, Henry Viets, then a fourth-year Harvard Medical School student, never forgot how he had "crossed the submarine-infested Atlantic . . . disguised as an embryo neurosurgeon . . . with *The Integrative Action* as my principal ballast" in order to work with Sherrington.[63]

The war must have affected the sensitive scientist's spirits as greatly as it did his work. A letter to an American friend, Dr. W. T. Councilman, dated April 16, 1916, suggests how deeply Sherrington was moved by the battle in Europe.

> To us here it is a very real source of comfort in this great European struggle to feel that we have the sympathy of Americans who know us . . . This country's unpreparedness for the war was partly due to its desire to show a peaceful attitude to Germany by refusing to believe, practically up to the last moment . . . that her armaments were for offence and aggression against her neighbors. This was, we all know — & know too late — an unwisdom. And terribly we have paid for the mistake, and are paying, & must still long pay almost unbearably dearly — lives upon lives, cut short in their flower and promise . . .
>
> One hideous surprise to us has been the inhuman licence & cruelty accompanying the German endeavour. At first we thought the reports exaggerated from Belgium and France. But the accumulation of evidence has been too great. And this last Wittenberg horror, it sickens me, perhaps because medical more even than all that has gone before . . . It is too bad to dwell on . . .[64]

With much of his own work disrupted, Sherrington threw himself into government war work with his customary drive and efficiency. He served on the Alcohol Committee of the Central Board of Control and the War Office Committee on Tetanus in 1916, publishing important observations on the use of anti-tetanus serum in 1917.[65] In 1918 he became chairman of the Industrial Fatigue Research Board. His study of industrial fatigue, begun at Liverpool, had been resumed in 1915 in war factories at the request of the War Office, and few episodes

better illustrate Charles Sherrington's character than his activities for three months during the summer of 1915.

He disappeared from home on a bicycle one day, presumably for a holiday, leaving no address. The need to replace a lost collar stud finally revealed his whereabouts: having decided to study fatigue *in situ* he was working incognito as an "unskilled workman" at the Vickers-Maxim shell factory in Birmingham. For eleven weeks the fifty-eight-year-old Sherrington lived in a workman's hut and worked the day shift, from 7:30 A.M. to 8:30 P.M. on weekdays and 8 A.M. to 5 P.M. on Sundays. "Our work," he later wrote to Alexander Forbes, "was mainly gauging and filling the shells and fitting on the fuse-sockets. Each shell contained 144 bullets and required over eighty separate processes." Upon his return to Oxford he reported with certainty to the War Office that shorter hours and improved living conditions would greatly increase productivity in the war factories! [66]

With the war's end Sherrington resumed his normal program of teaching and research, and, until near the age of seventy-five, performed one or more long experiments every week and spent many hours analyzing data. By his retirement in 1935 the "Sherrington School" at Oxford had issued a series of papers on topics such as after-discharge, summation, recruitment, postural contraction, and the motor unit, illuminating the finer details of the reflex activity of the spinal cord.[67]

Sherrington was not only a highly productive research scientist, but, like Michael Foster, he was able to recognize and develop talent in others and had long been interested in methods of teaching physiology. At Liverpool he had begun teaching some of the simpler classical experiments in mammalian physiology as a partial substitute for the many lengthy and often meaningless hours spent in frog nerve-muscle classes. After many years of trial and the use of one carefully guarded copy of typewritten notes, *Mammalian Physiology: A Course of Practical Exercises* was published in 1919. Carrying out Sherrington's belief in active student participation, the exercises in the book were accompanied by illustrations from students' class work, causing a foreign reviewer to complain that the "authorities"

quoted were all English. It was, in sum, a book which infused physiology with a variety of new teaching possibilities and led Adrian to comment of its author that "no laboratory could vie with the standards he set at Liverpool and Oxford." [68]

A second volume appearing in the post-war years was of a very different order from *Mammalian Physiology*. A slim volume of sixty-seven pages, *The Assaying of Brabantius* (1925) publicly revealed Sherrington the poet. The book, which carried a bare "C. S. Sherrington" on the title page, generally was well received by the critics. One reviewer, complimenting the book, advised Mr. Sherrington that, if he persevered, something might later be heard of him.[69]

As Sir Charles entered his eighth decade his enthusiasm for research work remained undiminished. His vigorous participation in laboratory affairs was evidenced during a program of papers, when he and Derek Denny-Brown demonstrated a monkey and read a report on the deafferented limb and cortical stimulation. Sherrington had arranged a rope going to the ceiling of the lecture room, with an apple at its top. As one of the audience recorded the scene, "the monkey made for the rope and apple rather before expectations, and it was a grand sight seeing Sir Charles hanging on the monkey's tail as it was trying to ascend. The Society was most enthusiastic." [70]

In February 1930, the seventy-three-year-old Sherrington was stricken with an alarmingly severe gastrointestinal attack. He was soon actively back to work, however, on projects such as the paper on motor units over which he had been laboring for two years.[71] "It is remarkable," Fulton wrote in his diary on April 2, 1930, "to see how at this time of his life he is beginning to correlate all the various aspects of his own work; structure of fibers, reflexes, series of central excitations, etc. etc., into a beautifully synthesized body of knowledge . . . [For him] the days simply weren't long enough, and there are all manner of things that need investigation. The rest of the world in his eyes is a little slow because it does not see all these things staring it in the face."

Two of the most outstanding events in Sherrington's last five years at Oxford were the First International Neurological Con-

gress, held at Berne in August 1931, and his receipt of the Nobel Prize in Physiology and Medicine in 1932. At the Berne Congress he and Harvey Cushing were surprised with honorary degrees. In awarding Sherrington's degree Professor Leon Asher ended his remarks with the now famous words, "Sir Charles, we look upon you as the supreme philosopher of the nervous system." Sherrington's presence at the Congress, a participant commented, "created a great stir. It was the first International gathering that he had attended since the War and many of the German neurologists fancied him dead. Asher's characterization of him . . . brought thundering applause and was probably the best thing said at the Congress. It reminded them that the man who had first formulated the modern interpretation of the nervous system was yet alive and walking among them." [72]

The Nobel award came to Sherrington specifically for his isolation and functional analysis of the single motor unit, a project he had labored over from 1928 through 1930. The award was shared with Edgar Douglas Adrian, Foulerton Professor of the Royal Society at Cambridge, "the pioneer whose work had the greatest immediate influence on the development of Sherrington's world of ideas." [73] Adrian's Nobel Prize was granted for his analysis of the frequency at which a single sense organ unit discharges. As was reflected by their joint receipt of the Nobel Prize, the Oxford and Cambridge neurophysiologists had been following converging routes in their motor and sensory studies, both seeking to define the properties of the nerve cell as a functional unit.

To many, especially those who had worked with him at Liverpool and Oxford, Sherrington's award was long overdue — a circumstance perhaps partly explained by the difficulty of citing a specific discovery on which to base the prize. For more than three decades Sherrington had sought to establish the nerve cell as the analytical unit of the nervous system, both structurally and functionally, a quest which was fully realized and recognized by the research on which the Nobel Prize was based. As Granit has justly said, the nerve cell as the analytical unit was "Sherrington's first great notion and for him, in a sense, it was journey's end." [74]

The honors that came to Sir Charles during his last years at Oxford were dimmed by the long illness of Lady Sherrington, who died on May 13, 1933. The words he wrote about "dear Ethel" to Harvey Cushing would apply equally well to himself as he endured a crippling arthritis nearly twenty years later. "Her gallantry and her patience never faltered to the last even for a moment . . . her spirit was always bright and indomitable." [75]

"RETIREMENT": 1935–1952

Although Oxford had no compulsory retirement age at the time of his appointment, Sherrington decided in 1935, at the age of seventy-eight, that the time had come to step down from the Wayneflete Chair. Leaving his home at Chadlington Road, he made the natural choice of Ipswich for his retirement years. Although his days in the laboratory had ended, Sherrington's work was not over. He served the Ipswich School as Governor and the town as an advisor on its museums and health services. As a trustee for the British Museum he acquired many rare and early books, which he presented to various National Libraries. In 1936, together with Lord Rutherford and Dr. Edmund Whitaker, he was named a member of the newly created Pontifical Academy of Science at Rome.[76]

These activities, however, were but appendages to Sir Charles's main concerns, for he now had time to become, in lectures and writing, philosopher and historian. Despite Asher's 1931 characterization of him as the "supreme philosopher of the nervous system," Sherrington had remained almost adamantly silent on what he saw as the philosophical implications of his work until near the end of his Oxford days. Those implications, to Sherrington, bore on one of philosophy's oldest and most controversial subjects, the relation of mind and body. Sherrington's "thinking cap" in this field, as Lord Cohen remarked, "was second-hand" — it had been worn by exponents of dualism since Descartes. One senses, however, that Sherrington was not a dualist by philosophical choice. Rather, it was a position he felt constrained to adopt because the sciences of his day offered no evidence, no means, for bridging the gap between mind and

brain. Sherrington first gave full expression to his dualism in his 1933 Rede Lecture on "The brain and its mechanism." "What right," he asked his audience, "have we to conjoin mental experience with physiological? No scientific right; only the right of what Keats . . . dubbed 'busy common sense' . . . The [mental and physiological], for all I can do, seem to remain disparate and unconnected." [77]

As Edinburgh University's Gifford Lecturer for 1937–38, Sherrington the biologist again became a philosopher and "turned from cat and chimpanzee to man." The lectures, published in 1940 as *Man on His Nature,* stressed his belief that "man is a product, like so much else, of the play of natural forces acting on the material and under the conditions past and present obtaining on the surface of our planet." [78]

For Sherrington the dualist, man is the product of natural forces yet encompasses a territory which neurophysiology could not reach — the realm of mind and thought. Discussing the problem of dualism shortly before his death he remarked, "some people think that thinking is all electric currents. Well!" [79] This in essence summarizes a dominant theme of the Gifford Lectures; for to the architect of the nervous system, thinking was something so different that it could not be fitted into the scheme of matter and energy that is used to explain material events in the nervous system.

Sherrington drew the materials for *Man on His Nature* from modern science and the history of ideas, and around them constructed his personal thesis. As he wrote to John Fulton, composing the book during the days of World War II deepened his sense of history, giving him an insight he would never forget.

> Namely, the cramped time-scale human history accustoms us to — we have got to free ourselves from that. I set the zodiac as headings of the chapters in order to help the reader to that; the old zodiac has changed merely a trifle since man first watched it. It puts our successive 'civilizations' into a perspective which does something to correct our notion of our own significance of late. Not but what it is of first importance of course that we should take ourselves seriously; but we have got to think more in terms of the stages of the planet's side. How 'cheep' [sic] & unimpressive all this 'sound and fury' of Nazi Germany seems as looked at under the old zodiac —

with the second law of thermodynamics peeping over 'Time's horizon.' [80]

The year 1939, Sir Charles's last year at Ipswich, was marked by two honors that touched him deeply. He was made an honorary fellow of Magdalen College, and he received a copy of his *Selected Writings,* a testimonial presented by the guarantors of the journal *Brain.* The book came as a complete surprise, and on receiving it he exclaimed, "how *did* they manage it?" [81]

In 1940 the eighty-three-year-old Sherrington was advised to move from Ipswich because of heavy aerial attacks. After an interlude in London, where even worse raids were encountered, he was persuaded by A. V. Hill to live temporarily in Cambridge. He moved into the Bull Hotel, which was promptly requisitioned, and next accepted the lodging offered by the Master of Caius. His stay at the Lodge was ended by a crippling attack of fibrositis, for which there was no permanent cure. After treatment at Droitwich, a Catholic nursing home, he was moved to Espérance, another Catholic home, at Eastbourne.[82] There, in a quiet house not far from the shore, he spent his last years, enjoying contacts with the masters and boys at Eastbourne School, receiving a constant stream of visitors, and continuing his writings.[83]

During the last four years of his life Sir Charles was troubled with deafness and largely confined to his room at Espérance by severe rheumatoid arthritis. His mind remained keen, and he continued to delight visitors with discourses on a wide range of topics and a never-failing supply of anecdotes about the people, places, and events he had known during his long career.

Six weeks before his death he complained to John Fulton that he had lived too long. But, added Sherrington "with his half-quizzical, mischievous, owl-like smile — 'at least I have outlived George Bernard Shaw.' " [84]

On the evening of March 4, 1952, in his ninety-fifth year, Charles Scott Sherrington died peacefully from heart failure. Of the scores of tributes which marked his death none more simply expressed the sentiments of those who knew him than the words of Dr. Henry Viets: "A great and good man has died . . . We stand on mighty shoulders." [85]

II

An Oriental Tale: Pre-Sherrington Studies of Reflex Action

Neurophysiology before Charles Sherrington has been likened to the oriental tale of four blind men who examined an elephant: one, seizing a leg, declared the elephant to be a kind of tree; another, grasping a tusk, held it to be a kind of spear; the third, feeling the trunk, said a kind of snake; and the fourth, holding the tail, pronounced it just a rope.[1] Each statement was a fair inference, but in sum they did not hang together.

Neurophysiologists' first clear, coherent perception of the "whole elephant" was provided by the concept of integrative action. This perception was, to an almost incredible extent, the result of Sherrington's labors alone. But many lines of investigation prior to his, piecemeal though they may have been, formed a pool of techniques, data, and theories from which he could draw in developing his paradigm for reflex motor behavior.

In this chapter, to set the stage for analyzing Sherrington's researches, we first will look briefly at various ideas about reflex action and its anatomical bases through the second half of the nineteenth century. We will then see how attempts were made to interrelate these inquiries in two British textbooks of physiology during the 1880's, when Sherrington was studying at Caius and beginning his researches.

REFLEX ACTION FROM DESCARTES TO HALL

The experimental study of nervous phenomena such as reflex motor action has little significant history before the seventeenth century. Yet from antiquity on, viewing motion as a primary sign of "life," men have speculated about the agency or agencies responsible for animal motion. Ancient writers were aware of the general distinction between voluntary and involuntary motions, and recognized that the nerves, spinal cord, and brain are somehow involved in effecting movement.

For centuries attempts to explain motor and sensory phenomena were influenced by the speculative concepts of "animal spirits" and "sympathy." [2] As described most fully in the theories of Galen (second century A.D.), "animal spirits," produced in the brain and sent to all parts of the body by unbroken conducting channels (the nerves), were the immaterial or subtle principle causing sensation and muscular motion. Physicians from the time of Hippocrates (c. 460–370 B.C.) were aware that the various organs and parts of the body are extensively interrelated. There is, they said in what might be seen as a prototype of the integrative action concept, a "sympathy" between parts of the body. "Sympathy," an immaterial psychic principle, could act directly or could unite parts of the body via a common blood supply or via the "animal spirits."

The enduring belief in immaterial agencies which are not amenable to direct study partly explains the centuries-long lag between descriptions of involuntary motions and their interpretation in neurophysiological terms. The foundations for the reflex action concept were laid in the seventeenth century with two major reorientations in the study of motor action and sensation. On a theoretical level, the way was paved for analyzing animal motion in terms of material causes by René Descartes' "bête-machine" concept. The body, in the Cartesian schema, acts as a machine and its motions are explicable in terms of the laws governing all physical machines. Secondly, as part of the resurgence of observation and experimentation characterizing seventeenth-century science, men began to amass information on the structure and function of nerves and muscles. Although limited by lack of techniques and by poor anatomical knowledge, their work began to show that the traditional theories of "spirits" and "sympathies" were inadequate to explain neuromuscular phenomena.[3]

By the mid-eighteenth century experimental work on the nervous system was separating into three main divisions, dealing with the spinal cord and reflexology, the brain as a neural structure, and the peripheral nerves. Accordingly, the study of "involuntary" or "vital" motions began to be the subject of specific researches, although it still lacked a vocabulary of its own.

"Reflex," for example, was used, as it had been by writers such as Descartes and Thomas Willis, as a passive verb: "animal spirits" were *reflected* by the brain or spinal cord through the nerves to produce motion, analogous to the reflection of light by a mirror. Thus, although the idea of reflex action was clear in many seventeenth- and eighteenth-century works, the word was not used to designate those unconscious and involuntary motions which we now recognize as "reflexes." [4]

The checks imposed on the establishment of the reflex action concept by lack of an adequate terminology are exemplified in the work of Robert Whytt of Edinburgh (1714–1766). Whytt's observations yielded data essential for understanding reflex actions, and he drew an almost complete picture of such actions; but his writings are couched in the language of volitional and conscious activities, of the "sentient soul" and of "sympathies." His numerous contributions to knowledge of reflex action, translated into modern terms, included (1) giving a remarkably complete list of specific reflexes and recognizing their protective functions for the animal, (2) noting that stimulus intensity influences response strength, and (3) recognizing, from experiments with decapitated and pithed animals (tortoises, frogs) that the spinal cord is a major locus for reflex action.[5]

By the end of the eighteenth century investigators had a workable knowledge of the reflex as an involuntary stimulus-response phenomenon. But knowledge of its structural bases had progressed little since the start of the century, and theorization, still largely concerned with finding how the "soul" operates in the body, continued to outstrip experimental fact. On the whole, each worker pursued his particular line of inquiry about the nature of involuntary motions, and few efforts were made to coordinate existing knowledge.

A notable exception to this uncoordinated state of speculation and research occurred in the treatises by Johann Unzer of Halle (1727–1799) and his former pupil Jiri Prochaska (1749–1820), a Professor at Vienna, who systematized existing knowledge of the nervous system.[6] An excerpt from Prochaska's 1784 treatise epitomizes the prevailing views of the nervous system and of reflex action at the start of the nineteenth century.

However composite the machine of the nervous system may be, I think it may be divided into three portions, just as its functions are most conveniently arranged into three divisions: namely, . . . the animal organs, or the organs of the mental faculty, the cerebrum and cerebellum; secondly, the general sensorium, which appears to consist of the medulla spinalis and medulla oblongata, together with that portion of the medulla of the cerebrum and cerebellum, from which the nerves directly arise; and, thirdly, the nerves distributed from the general sensorium to all parts of the body . . .

The reflexion of sensorial into motor impressions, which takes place in the sensorium commune, is not performed according to mere physical laws, where the angle of reflexion is equal to the action; but that reflexion follows according to certain laws, writ, as it were, by nature on the medullary pulp of the sensorium, which laws we are able to know from their effects only, and in nowise to find out by our reason. The general law, however, by which the sensorium commune reflects sensorial into motor impressions is the preservation of the individual . . . This reflexion may take place either with consciousness or without consciousness.[7]

By the time Sherrington began his researches, a century after Prochaska had written of "reflexion," study of the nervous system had become an increasingly specialized discipline. Areas such as reflexology, nerve transmission, cerebral localization, comparative neuroanatomy, and clinical neurology were evolving independently.[8] Two of Sherrington's most important nineteenth-century precursors, in terms of their understanding of the nervous system's coordinating capacities and of reflex action, were, respectively, the French physiologist Pierre Flourens (1794–1867) and the English physician Marshall Hall (1790–1857).

Physiologists, Flourens felt, had long been confused by observing two equally certain facts: the specialization of our organs, which creates functional diversity, and the subordination of this diversity to the unity of the organism.[9] He set out to resolve this confusion by determining the functions of the different parts of the vertebrate nervous system, chiefly the brain. In the first collection of his classic studies, published in 1824, Flourens analyzed the effects of destroying various portions of the nervous system in pigeons, dogs, and rabbits. One of his most significant findings was that the coordination of muscular

movements and locomotion in the normal animal is regulated by the cerebellum.[10] In 1900 Sherrington, so aware of the need to study the nervous system's "unifying" actions as well as the functions of its specific parts, evaluated Flourens' work as follows: "He translated the disturbances ensuing on destruction of the cerebellum to mean loss of a part possessing ability to co-ordinate the innervations which guide and execute complex movements. By his doing so, the idea of nervous co-ordination was, it seems to me, formally introduced into physiology." [11]

While Flourens was analyzing localization of function in the nervous system, Marshall Hall was studying involuntary motions in animals and man. Evaluating Hall's contributions to reflexology would require a monograph in itself. His writings were voluminous though often highly repetitive, and are difficult reading at best because of his endless neologisms and his tendency not to distinguish between his own work and that of his predecessors and contemporaries. Yet, controversial though he may be, Hall clearly made a number of fundamental contributions to both experimental and clinical knowledge of reflex action. In 1850 he introduced the term *arc* in connection with the sequence of functions involved in involuntary motion. The idea of an arc, plus Hall's insistence on a necessary connection in the nervous system between incoming and outgoing pathways, provided a basis for viewing the spinal reflex as a neural arc functioning independently of the brain.[12]

Among Hall's other achievements, translated into twentieth-century terms, were:

(1) vastly extending the category of reflex acts, including those of the autonomic nervous system;
(2) analyzing the effects of toxic agents on reflexes;
(3) naming the phenomenon of spinal "shock";
(4) demonstrating that tonic actions, such as the spinal frog's posture, are of reflex origin;
(5) using a spinal preparation, for perhaps the first time since Galen, to compare the reflex reactions of central and spinal segments;
(6) recognizing that an afferent impulse entering the spinal

cord has effects in the nervous system beyond an immediate segmental response;

(7) realizing, as seen in the spinal animal, that the spinal cord can be considered as a functional entity with a life of its own.

In such contributions, as a neurophysiologist stated in 1954, "can be found the basic ideas on which the present elaborations [of reflex actions] have been founded . . . by the work of Sherrington and his school." [13]

Workers from Descartes to Hall catalogued a great number of specific reflexes, began to define their characteristic properties, and recognized that their operation is a primary function of the spinal cord. But reflexologists on the whole devoted little attention to defining the structural mechanisms at the basis of reflex action, leaving such tasks to the anatomist and the histologist. The differentiation of the spinal cord's sensory and motor pathways and the study of nerve cells and their interconnections were two key lines of structural research for understanding the reflex functions of the spinal cord.

TOWARD THE NEURONE THEORY

Recognition of the structure of nerve cells and their interconnections, a story which is part of the evolution of the cell theory and improvements in histological methods, began in the 1830's with the development of the achromatic microscope. To microscopists of the 1830's it seemed that nerve cells, known as "ganglionic globules" or "corpuscles," and nerve processes had no clear or close connections with each other or with other structures. If this were true, they reasoned, a central locus and a peripheral locus are connected by only one nerve fiber. Thus a structure such as a muscle fiber would be related to only one point of the brain or spinal cord, making it extremely difficult to account for the obviously complex and coordinated nature of muscular movement.

A central concern of histologists from the 1840's through the 1880's, therefore, was to differentiate the types and components

of nerve cells more clearly and to determine the nature, if any, of their interrelationships. By 1845 it was recognized that some nerve fibers *might* come from nerve cells, but the nature, course, and the termination of these processes were obscure. "Some cells," wrote the English investigator R. B. Todd, "have tail-like processes," although one "cannot presently speculate on [their] use. . . . Do they constitute a bond or union between the nerve vesicles and certain nerve-tubes or are they commissural fibres serving to connect the grey substance of different portions of the nervous centres? . . . The great object of the anatomist's research," Todd continued, "should be to find out the precise manner in which the nerve fibres are united with the nerve vesicles, for the vesicular matter is the source of nervous power." [14]

In the 1850's, as seen in Rudolph Albert Kölliker's authoritative *Handbuch der Gewebelehre des Menschen,* knowledge of neural connections had not advanced greatly since the 1830's.[15] Kölliker noted that there was evidence that "pale-processes" (non-medullated fibers) might pass into "dark-bordered" (medullated) nerve fibers, and cautiously suggested that nerve anastomoses might exist.[16] Within a decade improvements in histological methods, such as the introduction of new stains and their systematic use and the use of paraffin and celloidin for embedding the semifluid, amorphous gray matter, greatly clarified this still vague picture of nerve cells and processes.

A major work in the history of histology, but one almost totally ignored by its author's contemporaries and successors, was Otto Deiters' (1834–1863) posthumously published *Untersuchunger über Gehirn und Rückenmark des Menschen und des Säugertiere* (1865). Deiters worked in Max Schutze's Bonn laboratory. By careful use of serial sections and the best stains available, he was able to distinguish clearly the axis cylinder from the "protoplasmic prolongations" (dendrites) of nerve cells, and to deny the existence of nerve anastomoses. His studies, further, left no doubt that nerve fibers originate in nerve cells — a fact that in time was known as "Deiters' Law." Camillo Golgi, using his silver impregnation methods, "proved" in 1873 what the forgotten Deiters had demonstrated: each nerve cell

has one prolongation in the form of an axis cylinder and many protoplasmic processes or "dendrites." [17]

The use of another major tool for unraveling the complex structure of the nervous system was pioneered by the English physiologist August Volney Waller (1816–1870) in 1850. Using the known and simple technique of cutting a nerve fiber, he concluded that axons degenerate when cut off from their cell bodies and that the latter are the axons' source of nutriment. Until the origin of nerve fibers from nerve cells had been fully accepted, and until the work of Marchi and Algeri in 1885, Waller's method could be accepted merely for what it showed — that when a nerve fiber is cut in two, one of the pieces degenerates. In the hands of Marchi and Algeri, who placed sectioned fibers in an osmic acid stain and fixative and found that the healthy fibers stained yellow while degenerating ones showed a row of black spots, the Wallerian method became a major means of tracing the origin and course of nerve fibers and tracts.[18]

Despite new methods for obtaining, preparing, and studying nerve cells and processes, the true nature of their interrelationships continued to elude nineteenth-century workers. On a macroscopic level the ancient idea of unbroken channels for the conduction of "animal spirits" found its early nineteenth-century counterpart in Charles Bell's concept of the "nervous circle": "Between the brain and the muscles there is a circle of nerves; one nerve conveys the influence from the brain to the muscle, another gives the sense of the condition of the muscles to the brain. If the circle be broken by the division of the motor nerve, motion ceases; if it be broken by the division of the other nerve, there is no longer a sense of the condition of the muscle, and therefore no regulation of its activity." [19]

On a microscopic level, an analogous belief in continuous pathways for the transmission of nervous excitation persisted into the early twentieth century, reaching its apogee in the reticular theory of Gerlach and Golgi. In 1858 Carl Ludwig, extending the ideas of Rudolph Wagner, depicted a nerve net in which fibers commingle at nodes, at each of which is a nerve

cell.[20] Moderate excitation, he suggested, enters one part of the net, passes through the node and nerve cell at its center, and travels from internode to internode until it reaches a muscle fiber. Stronger excitation, spreading farther throughout the net and engaging more fibers and internodes, ultimately excites more muscle fibers — a plausible view in the years before the all-or-none law.[21]

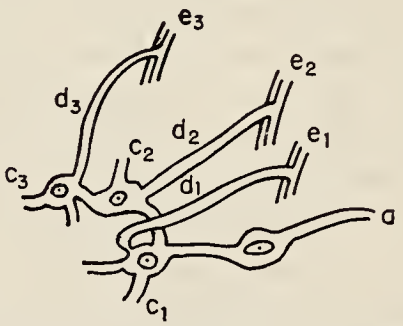

Fig. 1. *The Nerve Net — 1858.* According to Ludwig's theory, stimuli of increasing strength spread through the spinal centers of the "nerve net." Starting from *a* excitation can spread through the nerve centers to reach, first muscle fibers at e_1, then e_2, and finally e_3.

Echoing Ludwig's theory, Joseph von Gerlach used a gold chloride preparation and in 1871 saw what appeared to be an unbroken network of nerve fibers in the cerebrospinal axis. He hypothesized that nerve impulses are transmitted from cell to cell by the "neuropile," "nerve net," or "reticulum" composed of these anastomosing processes. The Reticularist School, of which Golgi assumed leadership, was challenged in 1886 and 1887 in papers by Wilhelm His (1831–1904), professor of anatomy at Leipzig, and August Forel (1848–1921), professor of psychiatry at Zürich. Wilhelm His reported that he could not see anastomoses when he observed stages in the growth of cell process from neuroblasts in haemotoxylin-stained embryonic tissue. Similarly, Forel stated that he could see no anastomoses, only blind terminations, in his Golgi preparations.[22]

Forel's and His's findings did little to rock the firmly entrenched reticular theory, but its foundation was soon undermined by the work of an unknown Spanish neuroanatomist and histologist, Ramón y Cajal (1852–1924), professor of histology at Barcelona. In 1888 Cajal had improved Golgi's stain and taken "a step amounting to genius" — the use of embryonic

material to avoid problems with metallic methods on the developed myelin sheath.[23]

To Cajal, study of the embryonic bird and mammalian cerebellum confirmed a theory he had been developing: although cells often do make contacts with other nerve fibers coming from many sources, definitely limited conduction paths exist in the gray matter, and nerve impulses are transmitted by contact or contiguity, not by the reticularists' continuity. Cajal's work transformed study of the functional anatomy of the vertebrate nervous system by revealing that it is built up of conductive chains of individually distinct and discrete conducting nerve cells. In 1891 H. W. G. Waldeyer published a conspectus of Cajal's theory, labeling it the "neurone theory."[24]

When Cajal presented his work at the October 1889 meeting of the German Anatomical Society in Berlin, he believed that his findings had discredited the reticular theory. But the Reticularists, under Golgi's able leadership, clung firmly to their beliefs, and the neurone theory was not firmly established until 1905–1906.[25] There is no more picturesque description of the long-lived reticular theory, and of the significance of the neurone theory for understanding the nature of reflex action, than that given by Cajal himself in his autobiography.

> [The reticular network is] a sort of unfathomable physiological sea, into which, on the one hand were supposed to pour the streams arriving from the sense organs and from which . . . the motor . . . conductors were supposed to spring like rivers originating in mountain lakes. This was admirably convenient, since it did away with all need for the analytical effort involved in determining in each case the course through the gray matter followed by the nervous impulse . . . the recticular hypothesis, by dint of pretending to explain everything easily and simply, explains absolutely nothing . . . the doctrines of reflexes, instinctive actions, functional localization in the cerebrum, etc., demand imperiously the recognition of perfectly circumscribed channels of conduction through the cerebrospinal axis.[26]

THE SPINAL CORD: SENSORY AND MOTOR FUNCTIONS

An analysis of reflex action that includes a correlation of function and structure demands a differentiation of sensory and

motor functions in the spinal roots and cord columns. From the time of Galen, who held that the presence of ganglia indicates that a nerve is "powerfully motor in action," the spinal root ganglia were recognized to be somehow involved in nervous processes. Understanding of the nature of this involvement advanced little until the 1780's, when several workers noted that a specialization of ganglia might indicate a specialization of function in the nerves on which they are located.[27]

With regard to the columns of the spinal cord, gross dissection, showing fibers grouped together in large bundles, had long suggested a division of function. One continuing though disputed view held that the anterior and posterior columns and spinal roots had different functions. Behind this suggestion lay the ancient idea, supported since the seventeenth century by the authority of Thomas Willis, that the brain is the origin of all the nerves and that the anterior and posterior roots and their respective columns are anatomically continuous.

In view of the uncertainties and conflicting opinions about the anatomy and function of the spinal roots and cord columns, it is little wonder that men such as Charles Bell in the first decades of the nineteenth century complained of the "extraordinary confusion" of the subject of the nerves and their roles in sensation and voluntary and involuntary motion. The confusion began to be dispelled by Bell's and Magendie's famous and long controversial studies, which showed that the anterior spinal roots have a motor function and the posterior roots a sensory function.[28]

The course of the Bell-Magendie discovery, apart from reflecting personality factors and national styles of scientific research, underscores the limitations that the lack of techniques and accurate anatomical knowledge imposed on neurophysiology throughout the first half of the nineteenth century. Because of these limitations controversy continued over the spinal roots and cord columns during the 1830's and 1840's. Every possible combination of functions seem to have been championed: (1) The anterior columns (*a*) control the flexors, (*b*) control the extensors, (*c*) control flexors and extensors, (*d*) control movement only, (*e*) transmit sensitivity, (*f*) are concerned with

"autonomic" functions such as anti-peristalsis; (2) the posterior columns are responsible for each of the preceding functions. As Liddell has observed, two reasons for the claims and counterclaims, apart from all other experimental variables, were the lack of standardization of stimuli used for testing sensation and the lack of checks upon the conditions and results of sepsis.[29]

The spinal roots and cord columns finally were separated, anatomically and functionally, by the discoveries of M. T. Schiff in 1850 and M. Brown-Sequard in 1855 — discoveries that resulted in another acrimonious priority dispute. By 1860 the conclusions that Schiff marshaled in his *Lehrbuch der Physiologie des Menschen* began to recast understanding of the anatomy and physiology of the spinal cord:[30]

(1) The posterior columns are not a bundle of fibers running from the posterior roots to the encephalon, and the cerebellum does not receive most of the sensitive fibers from the trunk and limbs.
(2) Section of the anterior, posterior, or lateral columns is followed by a certain degree of hyperaesthesia.
(3) The power of transmitting nervous excitation may exist in parts of the nervous system which are not excitable.
(4) Of fibers entering the cord by the posterior roots, some go up, others down; both conduct sensitive impressions and seem to go ultimately into the central gray matter of the cord or anterior columns.
(5) The transmission of sensitive impressions through the cord occurs in certain definite directions.
(6) Sensitive impressions made on any point of one lateral half of the body are transmitted to the sensorium by conducting elements distributed in all parts of the opposite lateral half of the cord.
(7) The gray matter of the cord seems to have an important share in conveying orders of the will to the muscles.
(8) The anterior columns of the cord have a great share in voluntary movement everywhere except in the upper part of the cervical region.
(9) Decussation of the conductors of voluntary movements seems to occur chiefly, but not entirely, where the anterior pyramids cross.

With the sensory functions of the posterior and motor functions of the anterior spinal roots clearly separated from the functions of the spinal cord columns — the latter a topic on

which much research remained to be done — two major aspects of spinal root neuroanatomy remained unclear. First, the question of what regions are innervated by the anterior root fibers: does a muscle receive its fibers from one or many roots? Second, an intrinsically more difficult task: the sensory fibers of the posterior roots had to be traced. Both of these problems were resolved by Sherrington's researches.

THE REFLEX FUNCTIONS OF THE SPINAL CORD

The disconnected strands of our narrative thus far appropriately reflect the historical development of functional biology. Growth of knowledge about the animal organism generally has proceeded through three often overlapping stages: the recognition of gross anatomical and functional features, a detailed study of structure and function, and a detailed correlation of structure and function. Until Sherrington's writings appeared, few attempts had been made, except by the authors of textbooks or analogous treatises, to correlate the details about reflex action, nerve cells, and the spinal cord's sensory and motor functions that generations of workers had amassed. Thus, to unify our narrative and to gain some idea of the consensus about the reflex functions of the spinal cord available to Sherrington, we will turn to two leading English physiology textbooks of the 1880's.

When Charles Sherrington matriculated at Caius College in 1880 Michael Foster's *Textbook of Physiology* was in its third edition.[31] Except for some figures added to the text this edition remained substantially the same as the first (1877), in which the section on "Reflex Actions" totaled a slim five and one-half pages. Volume three of the fifth edition, "The Central Nervous System," appeared in 1890 while Sherrington was lecturing on systematic physiology at St. Thomas's. In his preface to the volume Foster stated that "throughout the whole of this part I have been largely assisted by my colleague Mr. Langley, and by my friend and former pupil Dr. Sherrington. The latter, besides helping me with criticisms, has prepared for me most of the figures after original drawings by himself." In this

edition seventy-two pages were needed to describe the spinal cord, eighteen of which dealt with its reflex functions.

A second widely read work was Landois and Stirling's *A Textbook of Human Physiology,* valued by Sherrington as a beginner's text.[32] Although Foster's fifth edition and the Landois and Stirling text contained much new knowledge, they should be viewed as marking the end of an era in neurophysiology. They were written just before the "neurone theory" and the researches of Charles Sherrington reshaped understanding of the structure and function of the central nervous system.

The Anatomy of Reflex Action. As described by Landois and Stirling, the spinal cord was known to be composed of white matter externally and gray matter internally.[33] The gray matter, in the form of two "crescents," consists of an anterior and a posterior horn, a middle (lateral) part, and a commissure. The nerve cells of the gray matter, they stated, are arranged in four groups, forming more or less continuous columns: those of the anterior and posterior horns, the lateral (intermedio-lateral) column, and the posterior vesicular column of Clarke. The white matter, in turn, is arranged into anterior, lateral, and posterior columns by the passage of nerve roots to the horns, and consists chiefly of medullated fibers without the sheath of Schwann or nodes of Ranvier.

By the mid-1880's, as Foster observed, the development of techniques such as Wallerian degeneration, measurement of the areas of tracts at different levels, and study of tracts' developmental stages had enabled workers to distinguish the fiber tracts in the white matter's columns — columns which at first sight seem of uniform nature.[34] From sectional measurements of the tracts at different levels in the white matter's columns, Foster stated, "we may infer that each nerve has a representative of itself starting from the level of its entrance and running up to some part of the brain. Whether the fibres thus representative of the nerve are continuations of the very fibres of the nerve itself, or are new fibres starting from some relay of grey matter, with which the fibres of the nerve are also connected, is another question." [35]

New techniques also had begun to shed light on the functions of the white matter. "We may," Foster cautiously wrote, at least provisionally infer that while "considerable portions of both the anterior and the posterior columns are like the adjoining grey matter in some way or other concerned in the exit and entrance of efferent and afferent fibres, the larger portion of the lateral column is concerned in the transmission of impulses to and fro, between the local mechanisms below, immediately connected with the several spinal nerves, and the brain above." [36]

Foster, and Landois and Stirling, devoted major portions of their discussions of the spinal cord to the gray matter, for here, workers realized, lay the bases of the cord's functions. In thoroughly reticularist terms, the gray matter was described as containing "an exceedingly delicate fibrous network of the finest nerve fibrils [*Gerlach*], which is produced by the repeated division of the protoplasmic processes of the multipolar ganglionic cells. Medullated fibres traverse and divide in the gray matter and become non-medullated; some of them merely pass through the gray matter of the non-medullated fibres and terminate in Gerlach's network." [37]

"The great feature of the nerve cells of the central nervous system," Foster felt, "is the remarkable way in which their processes branch off into delicate filaments." But techniques in the 1880's still were not refined enough to reveal the precise nature of this branching. Foster could only assert that the posterior root's afferent fibers "are in some way by means of the grey matter" brought into connection with the anterior root's efferent fibers.[38]

As he had done in his first edition, Foster likened the spinal "centres" uniting afferent and efferent fibers to a "sort of molecular machinery." He emphasized that he had purposely used the word "centre," avoiding mention of "nerve cells." But, Foster continued,

> undoubtedly the part of the spinal cord acting as centres of reflex action is situated in the grey matter, which . . . is characterized by the presence of nerve cells; undoubtedly also the efferent fibres are connected with the afferent fibres by means of cells . . . So that

a reflex action is carried on undoubtedly *through* cells . . . The power of carrying out a reflex action is probably contingent on the nature and arrangement of axis-cylinders, and of the branching material by which in a nerve centre the afferent and efferent axis-cylinders are joined together, the nuclei intervening only so far as they have to do with the growth and repair of nervous material.[39]

Summarizing the major facts which he presented about the spinal cord's structure, and "always keeping in view their physiological meaning," Foster concluded that "the important feature of the spinal cord is the presence of what we have called 'grey matter,' and all our knowledge goes to show that the important powers of the spinal cord, by which it differs from a thick multiple nerve, and by virtue of which we speak of it as a nervous centre or series of centres, are in some way or other associated with this grey matter." In contrast to the ganglia of the "splanchnic system," which seem to have no "marked transforming power over the impulses passing along the fibre," the gray matter of the spinal cord is "especially characterized by the possession of reflex and automatic as well as other powers." [40]

Reflex action. "Reflex action," Michael Foster had written in the first edition of his *Textbook,* "may be said to be, *par excellence,* the function of the spinal cord." His discussion of these functions in the fifth edition opened with valuable words of caution to students. In studying the isolated spinal cord or one of its segments one "must greatly hesitate to take it for granted" that the work it can do "is the work which is actually done in the intact body when the brain and spinal cord form an unbroken whole." In pointing out that the brain normally works via the spinal cord and the cord functions under the brain's control, even though the two are anatomically separable, Foster emphasized a fact too often ignored by his contemporaries: the nervous system is a functioning unit.[41] This fact was to be underlined and in large measure explained by the concept of integrative action.

A second experimental difficulty, Foster warned, arises through operative interference with the central nervous system. While the nature of shock was not yet fully understood, it was

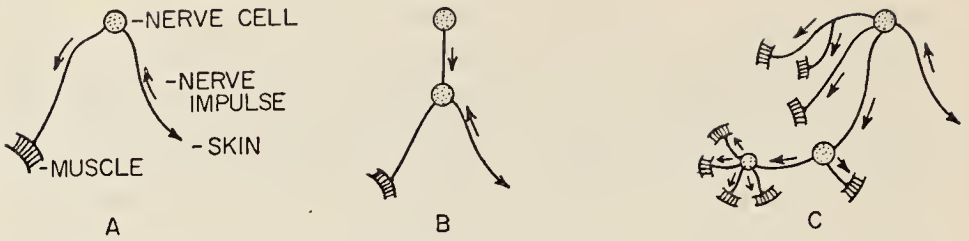

Fig. 2. *Elementary Connections in the Nervous System — 1858.* (*A*) Reflex Action. (*B*) Inhibition. (*C*) Eradiation.

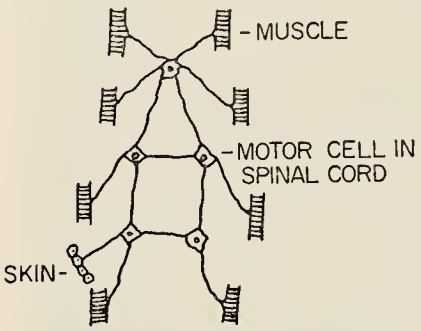

Fig. 3. *Scheme of Propagation of Reflex Activation (1887; compare with Fig. 1.)*

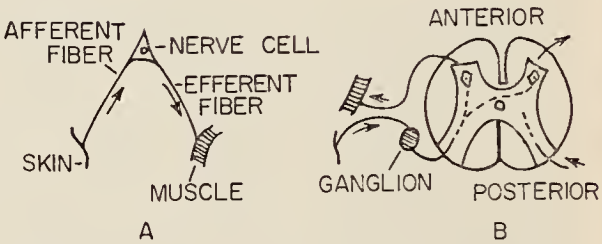

Fig. 4. *Reflex Arc Connections — 1887.* (*A*) A Reflex Arc. (*B*) Section of a spinal segment, showing a unilateral and crossed reflex act.

VIEWS OF REFLEX PATHWAYS

known that a spinal cord section may temporarily suspend reflex activity, that the phenomena conspicuous soon after sectioning may quickly disappear, and that activities at first absent may later reappear.[42]

A third problem, reflecting the "great differentiation of the central nervous system in the higher animals," was the fact that mammalian reflex phenomena may vary greatly in different species, in different individuals, and in the same individuals under different circumstances. Referring to this variability in the third edition, Foster in retrospect seems to have sounded a call for Charles Sherrington when he stated, "It is evident that the reflex as well as other phenomena of the mammalian spinal cord present a large field for inquiry, being much more varied and extensive than previous experience had led us to believe." [43]

On the eve of the neurone theory, the machinery for a "purely reflex act," in which "all voluntary activity is excluded," was

pictured as consisting of three anatomically continuous elements: a centripetal or afferent fiber, a "transferring" spinal center, and a centrifugal or efferent fiber (Fig. 2). Reflexes were divided into three major groups: (1) superficial — excited by stimulating the skin, such as a plantar reflex; (2) deep or "so-called tendon," such as the knee jerk; (3) organic, such as acts of micturition and defecation and acts connected with motor and secretory digestive processes, respiration, and circulation.[44]

Within each of these three groups, in turn, three classes of reflex movements had been catalogued: (1) simple or partial, in which stimulation of a sensory area effects movement in only one muscle; (2) extensive incoordinate, in which movements are in the form of clonic or tetanic contractions; (3) extensive coordinated, due to the stimulation of a sensory nerve causing discharge of complicated reflex movements in whole groups of muscles.[45]

From the time of Whytt normal reflex movements ("simple" or "extensive co-ordinate") in both cold- and warm-blooded animals had been recognized as purposeful and coordinated in nature. By the 1880's a complex of four factors had been isolated as the principal determinants of these characteristics: (1) the characteristics of the afferent impulse, (2) stimulus intensity (recognized as an aspect of no. 1), (3) stimulus locus, and (4) the "intrinsic conditions" of the spinal cord — the "exaltation" or "depression" of its normal "explosive energy." [46]

In ordinary stimulation of the skin, Foster noted, a series of afferent impulses, not a single impulse, pass upward along a sensory nerve. In fact, he stressed, "in every reflex action . . . the central mechanism may be looked upon as being thrown into activity through a *summation* of the afferent impulses reaching it" (italics added).[47] During the period of summation reflex actions do not simply pass through the spinal centers but are "profoundly modified," accounting for the fact that a reflex action's time is always much longer than that taken up by the passage of a nerve impulse along a nerve fiber. Thus, Foster observed, "reflex action" is an unsuitable term, because "the afferent impulse is not simply reflected or turned aside into an efferent channel; on its arrival at the centre it starts changes of

a different nature from and more complex than its own; and the issue of efferent impulse is the result of those more complex changes not the mere continuation of the simpler afferent impulse . . . Many processes, of which we have at present very little exact knowledge, are being carried on." [48]

Stimulus locus, too, was recognized as profoundly affecting the nature of a reflex action. Prior to Sherrington's researches, the four "laws of reflex action" proposed by Eduard Pflüger in 1853 were accepted as the definitive statement of the effects of stimulus locus. According to Pflüger:

(1) The reflex movement occurs on *the same side* on which the sensory nerve is stimulated, while only those muscles contract whose nerves arise from the same segment of the spinal cord.
(2) If the reflex occurs on the *other* side, only the corresponding muscles contract.
(3) If the contractions be unequal upon the two sides, then the most vigorous contractions always occur on the side which is stimulated.
(4) If the reflex excitement extends to other motor nerves, those nerves are always affected which lie in the direction of the medulla oblongata. Lastly, all the muscles of the body may be thrown into contraction.[49]

Analysis of the factors shaping a reflex action, Foster pointed out, shows that every segment of the nervous system is mapped in mechanisms directing certain afferent impulses into certain efferent channels.[50] The nervous network, he added, is not a fixed, rigid arrangement, for one cannot predict exactly the resulting reflex movement, and under certain conditions a movement different from the normal one may appear. In this observation we see the growing awareness that a reflex is a complex, variable act rather than a fairly simple, mechanical stimulus-response sequence. Two kinds of afferent impulses, Foster continued, seem to be involved in any usual reflex action: the ordinary afferent impulses which discharge the nervous mechanism within the cord, and the afferent impulses which connect that mechanism with the muscles about to be activated, and which take part in the coordination of the movements provoked. Again seeming, in retrospect, to sound a call for

Sherrington's analysis of muscle management, Foster admitted that

> the nature of these latter afferent impulses is at present obscure; we know as yet little more than the fact of their existence; but if we admit, as we seem compelled to do, that the character of a reflex action is determined by them as well as by the afferent impulses which actually discharge the mechanism, it seems possible that a fuller knowledge of these coordinating afferent impulses may afford an adequate explanation of the fact that when . . . the usual set of muscles cannot be employed by the nervous mechanism, recourse is had to another set.[51]

In discussing the reflex functions of the spinal cord, Landois and Stirling and Foster cited many phenomena which were of growing interest to physiologists at the end of the 1880's, and which became foci of Sherrington's researches in the decades to come. *Reflex time,* a crucial point in the debate over the nature of the knee jerk, was defined as "the time necessary for transferring the impulse from the afferent fibre to the nerve cells of the cord, and from them to the efferent fibre." [52] To test for reflex excitability and estimate reflex time, Landois and Stirling described, for want of a better technique, Türck's method (1851) of dipping a pithed frog's foot in dilute sulphuric acid and noting the time before withdrawal.

Another little-understood phenomenon, already noted, was *summation of stimuli,* and its relation to *graduated reflex responses.* The phenomenon of *muscle tonus* was recognized but its exact nature and meaning were in dispute. Foster discussed tonus under the "automatic actions of the spinal cord," concluding that its maintenance is one of the cord's functions and that it "presents many analogies with a reflex action." Landois and Stirling, on the other hand, sided with those denying the reality of tonus as an automatic function of the cord. If the phenomenon exists at all, they held, it is a reflex action.[53]

The occurrence of central nervous system inhibition, which Sherrington would show to be fundamental in integrative action, was also recognized. But beyond the experiments of Setchenov (1863) on the existence of an inhibitory center in the brain, and analogies made from the better-understood in-

stance of vagal inhibition of the heart, little could be said about central inhibition. Foster in 1890 could only state that "in all probability, actions or processes, which we may speak of as inhibitory, do play . . . an important part in the whole work of the central nervous system; in all probability many of the phenomena of nervous life are the outcome of a contest between what we may call inhibitory and exciting or augmenting forces." [54]

In summary, as neurophysiological knowledge stood in the 1880's, many of the structural and functional bases of muscle management, particularly at the spinal level, were at least recognized in principle if not understood operatively. Although interpreted in terms of the reticular theory, the structure of nerve cells and processes and their groupings in the gray and white matter of the spinal cord had largely been recognized. Precise mapping of the sensory and motor pathways served by the spinal root fibers awaited Sherrington's analysis.

Functionally, it was known that a reflex motor act is a complex affair shaped by a number of factors, including the character of the afferent impulse, the stimulus locus, and, principally, the events occurring in the spinal cord's "nervous centers." That these latter events were complex was obvious, but *what* they were was far from clear.

In 1890, before the language and principles of the neurone theory and understanding of phenomena such as reciprocal innervation, common paths, and central excitation and inhibition had come into being, an authority like Michael Foster could only inform his readers that

> The nerve centre may be regarded a a collection of explosive charges ready to be discharged and so to start efferent impulses along certain efferent nerves . . . a centre concerned in reflex action is to be regarded as constituting a sort of molecular machinery, the character of the resulting movements being determined by the nature of the machinery set going and its condition at the time being, the character and amount of the afferent impulses determining exactly what parts of and how far the central machinery is thrown into action.[55]

III

A Preliminary Step: Anatomical Studies (1884–1898)

Short questions notoriously may take long answers.
— *Jean Fernel*

Neurophysiologists have developed three main ways to study the operations of the nervous system: (1) mapping sensory and motor pathways by tracing the connections of different fibers and cell groups; (2) determining the functions of different parts of the nervous system, such as the cortex, brain stem, and spinal cord, and their relation to the system as a whole; and (3) analyzing the simplest activities of the nervous system by means of a detailed study of reflexes.

The bulk of Sherrington's researches involved the second and third methods, centering about study of the reflex functions of the spinal cord. At the outset of his investigations, however, he found that he had to take a "preliminary step." For a decade of what seemed to him often "boring" and "pedestrian research" [1] he surveyed the whole field of distribution of each spinal root, in order to create a sound anatomical foundation for his functional studies.

FIRST RESEARCHES: THE CORTEX AND PYRAMIDAL DEGENERATIONS

Sherrington's first ventures into neurophysiological research, as noted earlier, were occasioned by Goltz and Ferrier's 1881 debate over localization of motor control in the cortex. Sherrington became interested enough in the problems of brain-cord connections to spend the winter of 1884–85 on his George Henry Lewes Studentship, working at Strasbourg with preparations supplied by Goltz.

From the studies at Strasbourg came Sherrington's first solo scientific paper, which contained the first experimental determination of the region of the dog's cortex in which injury causes pyramidal tract degeneration. The paper also included

the first of many terms he introduced into neurophysiology and his first recorded observations on the study of neural function during life.[2] A second paper on the cortex and pyramidal tracts, appearing in 1889, marked several crucial turning points in Sherrington's scientific career.[3] He began to perform his own operations upon dogs and monkeys rather than use preparations supplied by others, and in the tradition of David Ferrier he chose to work primarily with the more complex corticospinal field offered by the monkey. After 1889, he began to subsume structural problems under problems of functions. Finally, and most significantly, by 1889 Sherrington had come to realize, largely through Gaskell's influence, that his research had "begun at the wrong end" — with the cortex and pyramidal degenerations — and that the spinal cord with its obviously simpler structure offered a better field of attack on functional problems.

THE NATURE OF THE KNEE JERK

When Sherrington turned his attention to the spinal cord, the first object of his investigations was the knee jerk, a phenomenon readily elicited by sharply tapping the quadriceps (extensor) muscles or the patellar tendon of the leg. His studies of the knee jerk began in the physiology laboratories of St. Thomas's Hospital, where he was serving as a lecturer in systematic physiology.

The knee jerk had first been described clinically, independently and in the same journal, by W. H. Erb and C. I. O. Westphal in 1875.[4] From the beginning, opinions were sharply divided over the nature of the knee jerk, although it was recognized as a useful diagnostic tool in clinical neurology. Erb asserted that the response which follows stimulation of the patellar tendon was a "true tendon reflex" (involving neural conduction to the cord and back), and Westphal claimed that it was a direct mechanical twitch of the muscle (an idiomuscular contraction), with a state of tonus in the muscle being a necessary condition for its occurrence.

A number of workers soon supported Erb's reflex theory by showing that the jerk is dependent on a spinal reflex arc,

but did not eliminate Westphal's theory of the role of tonus.[5] The major objections to the reflex theory of the knee jerk were that the jerk did not show "purposiveness," [6] was not affected by narcotics, was not inhibited but only affected by the action of opposing muscles, and, chiefly, that the time between stimulus and response (latent period) was too brief to permit conduction to and from the spinal cord. [7]

Another aspect of the knee jerk observed by almost all early workers and of special interest to Sherrington was its variability. As Fearing commented, "The possibility that the course of the [jerk] was modified by simultaneously activated neuromuscular mechanisms suggested itself as an explanation of the observed variability. The study of inhibition and facilitation had antedated the discovery of the knee jerk, and it is not surprising that [it] should have been considered in the light of these investigations." [8] Investigators such as Mitchell and Lewis in 1886, Lombard in 1888, and Bowditch and Warren in their classic paper of 1890 reported on the changes in the normal knee jerk produced by variables such as voluntary movement, hunger, fatigue, music, strong emotions, and sensory irritations. Lombard closed his report with the pregnant observation that "the causes of these variations of the knee-jerk are not only alterations in the muscles and nerves involved in the process, but, to a still greater degree, changes in the activity of the central nervous system, either as a whole or in part." [9]

When Sherrington entered the arena of debate over the nature of the knee jerk he directed his attention toward the basic question of the muscles and nerves upon which the jerk depends — an approach that had not engaged clinicians, who were using the jerk as a diagnostic tool and studying its time relationships and variability. Working with the monkey, Sherrington reported three essential findings in 1891:[10] (1) the extensor spasm constituting the jerk depends almost exclusively upon the vastus internus portion of the quadriceps extensor muscle and the internal portion of the crureus (intermedius) muscle; (2) the reflex arc upon whose integrity the jerk and the tonus of its muscles depend involves the fifth lumbar posterior spinal root and the fourth and fifth lumbar anterior spinal roots;

(3) within these roots the only fibers requisite for the jerk are the sensory fibers from and the anterior crural motor fibers to the vastus internus and crureus muscles — the muscles controlling the jerk (Fig. 5).

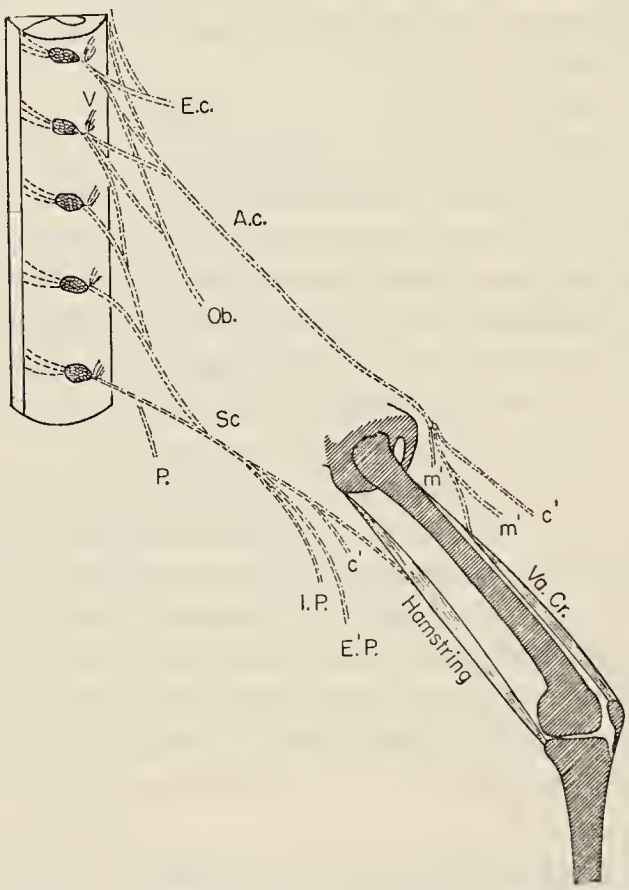

Fig. 5. *The Knee Jerk.* (*E.c.*) External cutaneous nerve trunk. (*A.c.*) Anterior crural nerve trunk, with *c*, cutaneous, and *m'*, muscular, branches. (*Ob.*) Obturator nerve trunk. (*Sc.*) Sciatic nerve trunk, with *I.P.*, internal popliteal, *E.P.*, external popliteal, divisions, and the division going to the hamstring muscles, which gives a cutaneous branch *c'*. (*Va. Cr.*) The vasti and the crureus muscles, the internal portion being especially referred to.

While he was studying factors abolishing or enhancing the knee jerk, Sherrington's attention was caught by two small but significant observations that eventually would lead to his study of sensory pathways and his reshaping knowledge of the sensibility of muscles. First, he found that passing a thread around the posterior nerve root of lumbar V prevents the jerk but does not

obviously impair conductivity in the sensory fibers passing from the skin in the same root. Second, Sherrington discovered that the jerk is exaggerated by sectioning that part of the sciatic nerve innervating the hamstring muscles at the back of the thigh. That the exaggeration has a physiological rather than a merely mechanical significance, he reasoned, is seen in the fact that increasing the tonicity or tension of the hamstring by stimulating the central cut end of the sciatic causes abolition of the jerk.[11]

As was pointed out in Chapter II, once the sensory functions of the posterior and motor functions of the anterior spinal roots had been established, a major question confronting neuroanatomists was the distribution of the sensory and motor fibers themselves. In his first studies of the knee jerk, Sherrington found that he could not deal satisfactorily with functional problems, such as the mechanisms abolishing or enhancing the jerk, in the face of this great gap in anatomical knowledge. What spinal roots, spinal segments, and motor and sensory pathways were involved in the knee jerk?

> At the commencement of some observations on the reflex mechanisms of the spinal cord in the Monkey, I was met by difficulties which made it desirable to attempt for that animal a somewhat particular examination of the distribution of the efferent and afferent spinal nerve-roots belonging to the lower half of the body . . .
>
> For the study of the functions of the spinal cord, it is of importance to know accurately the positions of the central and peripheral structures between which the fibres of the spinal nerves constitute links.[12]

MOTOR PATHWAYS

Sherrington began his decade-long attack upon these anatomical questions with an examination of motor pathways, chiefly those in the lumbo-sacral plexus. He published his findings in 1892 in a "Note" of 150 pages.[13]

The nature of motor innervations. Sherrington's interest in motor pathways had been stimulated not only by his knee jerk studies, but also by a paper published in 1881 by Ferrier and

Yeo. Examining the muscular combinations evoked by electrical stimulation of motor roots in the monkey, they had concluded that the complex of efferent fibers gathered together in each motor root is the result and representative of a "highly coordinated functional synergy." If Ferrier and Yeo were correct, Sherrington felt, then "analysis of the motor root will . . . mean analysis of a functional motor combination of high physiological significance." [14]

Since the earliest physiological experiments on motor pathways to the lumbo-sacral plexus by Bartholomeo Panizza in 1835, opinions had been sharply divided on whether the plexus had an anatomical or physiological significance. Two other equally important and controversial topics were whether the primitive nerve fibrils actually fused in a plexus, and whether the anterior root fibers served one or many muscles. Combining anatomical and physiological studies of the brachial and lumbosacral plexuses of frogs, rabbits, and humans, Heinrich Kronenberg in 1836 showed definitively that the primitive nerve fibers do not actually fuse in a plexus. The first step toward answering the question of whether the fibers of an anterior root serve one or many muscles was taken by Eckhard's study of the frog's sciatic plexus (1849) and Peyer's work on the rabbit's brachial plexus (1853). In these animals, they found, one muscle receives fibers from many roots, and there is a good deal of variation in the limb movement evoked by stimulation of a given nerve root among animals of the same species.[15]

Ferrier and Yeo's paper (1881) marked the next major contribution to knowledge of motor innervations in limb plexuses. Five years later, reporting on naked-eye dissections of the brachial plexus in fifty human beings, W. P. Herringham formulated two "laws" of motor distribution which also guided Sherrington's study:

(1) Any given fibre may alter its position relative to the vertebral column but will maintain its position relative to other fibres.
(2) Of two muscles or of two parts of a muscle, that which is nearer the head end of the body tends to be supplied by the higher, that which is nearer the tail end by the lower nerve. Of two muscles that which is nearer the long axis of the body tends to

> be supplied by the higher, that which is nearer the periphery by the lower nerve. Of two muscles that which is nearer the surface tends to be supplied by the higher, that further from it by the lower nerve.[16]

Sherrington's "Notes". When Sherrington began his study of motor pathways, he realized that the methods of dissection and descriptive anatomy were not adequate to unravel the complexities of nerve filaments to and within the lumbo-sacral plexus. He therefore turned to physiological experiments, working with the frog, rat, rabbit, cat, dog, and monkey (*Macacus rhesus*), using the first five animals chiefly for comparative purposes.

The detailed discussion of experimental methods in Section II of his "Notes" reveals the use of the simple techniques which, combined with his own operative skill and faculties of observation, characterized Sherrington's work. Sherrington's two chief pieces of apparatus, which in his hands became major tools for the study of reflexes, were the isotonic myograph and the inductorium. The latter, as Ferrier had found, was vastly superior to the commonly used voltaic battery (which simply caused a muscular twitch upon opening and closing the circuit), for "faradic" (induced) current provided repetitive stimulation.

Sherrington had as a guide for practical laboratory methods the works of Étienne Marey (1830–1904), a professor at the College de France. He learned of Marey's methods from the work of Marey's pupil, François Franck, who in 1887 published a study on the use of the myograph for recording the results in muscles of stimulating the dog's cortex. Prior to Marey's and Franck's work, the myograph had been used mainly for recording the contractions in isolated nerve-muscle preparations of the frog. Sherrington's use of the myograph in his lumbo-sacral plexus studies opened another new field for graphic recording, that of analyzing reflex actions.

Sherrington's basic technique for mapping motor pathways consisted of anaesthetizing an animal, exposing the spinal canal, and isolating the individual nerve roots. The distribution of the fibers of an isolated motor root was then analyzed by observing which muscles contracted when the fine filaments of the root

were individually excited. Always aware of the possible sources of error in physiological experimentation, Sherrington guarded against the escape of current from the inductorium, which could distort his excitation studies, and further checked his data by running a series of control experiments.[17]

In the course of root excitation and root severance experiments, Sherrington found that the frequency of individual variation, for both the anatomical and physiological constitution of the efferent roots, was great enough to warrant the introduction of two anatomical terms that are now standard. A plexus and its trunks and branches are *prefixed* if they contain spinal root-filaments attached to the cord further headward than are the root-filaments entering the corresponding trunk and branches of a converse class of plexus, the *postfixed.*

Having made this important distinction and confirmed its presence in the frog, cat, and monkey, Sherrington devoted Section III of his "Notes" to discussing the distribution of motor roots to muscles other than those of the limbs, such as those of the anus, vagina, and bladder. Then, in Sections IV, V, and VI, he analyzed the relation of the limb to cell groups in the cord, the significance of the arrangement of the limb plexus, and the general features of motor nerve-root distribution to the limb musculature. The scope of the structural and functional observations presented in these sections shows clearly the variety of topics occupying Sherrington's mind at the time, but we will note only his most general findings as they bore on his studies of the reflex functions of the spinal cord.

On the basis of his study of the monkey's lumbo-sacral plexus, Sherrington decided that the primary function of a plexal arrangement is to sort and collect nerve fibers passing through a number of spinal roots from an extended line of origin in the cord. As a result of the collection, all those fibers destined for a given muscular organ are gathered together in one and the same nerve trunk. Supported by numerous lines of evidence, Sherrington thus upheld a thesis advanced by Johannes Müller in 1834, "attributing to the arrangement of the motor roots of the limb plexus an anatomical significance based on metamerism rather than a teleological one dependent on supposed demands of

functional coordination . . . a hope with which the experiments in this paper were commenced is therefore disappointed. By analysis of the complex of fibres constituting the motor root one does not necessarily arrive at analysis of the muscular combination habitually employed for some particular coordinate movement of the limb." [18]

Regarding the scheme of motor nerve-root distribution to the limb musculature, Sherrington's analysis confirmed Eckhard's and Peyer's view that a limb muscle obtains nerve fibers from several (usually two or three) nerve roots. Secondly, Sherrington discovered that the muscles innervated by the same nerve root usually lie adjacent to one another, so that a continuous sheet or band or ray of muscular tissue is supplied by the same nerve root.[19] Within each anterior spinal root, in turn, the motor filaments are arranged so that stimulation of any constituent filament usually gives the same qualitative result as does stimulation of the entire root. "In other words," Sherrington explained, "the commingling of the motor fibres to various muscles is great even at their very exit from the cord, and each of the natural rootlets of the root consists of an aggregate of fibres often representing as far as the skeletal muscles are concerned all the groups of nerve-fibres contained in the entire root." [20]

Sherrington's study included a detailed mapping of the region of outflow from the spinal cord motor roots to the limbs in the rat, cat, dog, and monkey. In the course of this mapping work, he uncovered an important morphological feature of the spinal cord which provided valuable guidelines for determining reflex pathways. The region of outflow, he observed, "often ends not conterminously with the spinal segment but somewhere within the spinal segment either as it were overstepping or falling short of the anatomical limits of a segment. The representation thus stops short not at the interval between two segments of the cord, but midway within a segment of the cord. This fact may modify considerably our conception of the spinal root as a guide in studying the segmental arrangement of the limb, and on the other hand our conception of the morphological construction of the limb itself." [21]

Another important outcome of the motor root mapping was confirmation of Eckhard's observations on individual variation. In the monkey, Macacus, Sherrington found, excitation of the same spinal nerve root does not always evoke the same movement, even in individuals of the same species, age, and sex. Studies of variation also substantiated Herringham's first law, which Sherrington viewed as "the earliest statement of an important truth." [22]

Having presented his exhaustive analysis of motor pathways, Sherrington turned in the final four pages of his "Notes" to the general morphology of the mammalian limb as revealed by the distribution of its motor nerves. After reviewing the schemes of earlier workers, and noting that Herringham's second law does not appear to apply to the musculature of the posterior part of the leg and thigh, he summarized his own observations on the monkey, which pointed "to the limb being composed of a number of rays placed at right angles to the longitudinal axis of the body and parallel with the long axis of the limb. The most posterior of these muscular rays are the longest ones, and the most anterior the shortest ones of the limb series . . . Broadly described the musculature of the limb is built up by successive combinations of segments." [23]

SENSORY NERVES IN MUSCLES

One of the many problems that engaged Sherrington's interest in his studies of the knee jerk and of motor innervations was the existence of sensory nerves in muscles.[24] Recognition of the body's need for a "muscle sense" goes back at least to the time of Aristotle, when touch and muscular sensibility were confused. Descartes, in the seventeenth century, was aware of the fact that sensations are aroused by limb movements, and Charles Bell in 1826 had postulated the "nervous circle" to provide an apparatus for the muscle sense. Writing in 1842, the French physiologist François Longet had clearly depicted the role of muscular sensibility in the animal economy:

There is no doubt that the first condition for harmony in muscle movement is the sensation of its accomplishment. In fact, how could

a man or animal who has lost sensation of movement of limbs, who cannot judge of their attitude, or their relations with external objects, who does not know, as it were, even if they exist, who does not feel the ground with the limbs placed upon it, how could such a being walk with regular movements, preserve his equilibrium, and make the limbs work with full energy, promptitude, and characteristic harmony? [25]

Sherrington noted in 1894, at the start of his first, and fundamental, paper on the subject, that in spite of this long-recognized need of a muscle sense, "anatomical evidence of the existence of afferent fibres in the nerves distributed to skeletal muscles remains but scanty, [and] some authorities question the validity of the sparse observations which supply it." [26] His attempts to remedy this situation, he commented, were first stimulated by conversations with A. D. Waller in 1891.[27] Subsequently, his knee jerk experiments convinced Sherrington that the branches of the anterior crural nerve to the vastus internus muscle, and the branches of the sciatic nerve to the hamstring muscles, *must* contain afferent fibers, and he set out to identify them and see whether they were a unique case.

By 1894 he had answered these queries, after having conducted a series of twenty-four detailed experiments with cats and monkeys. Using two chief techniques, nerve degeneration and histological analysis of the number, size, and distribution of the myelinate nerve fibers remaining undegenerate, he found that from one-third to one-half of the myelinate fibers in a motor nerve trunk do not undergo degeneration after section of the motor root. The undegenerate fibers, he showed, come from cells of the posterior spinal root ganglia and so are sensory in nature.

With this data in hand Sherrington could state conclusively that "macroscopic nerve-trunks are as regards their myelinate fibres in no case purely motor. All are sensori-motor or purely sensory." [28]

He thus had answered, in full measure, his original questions, identifying the afferent fibers in the anterior crural and sciatic nerve branches and showing that the constitution of the anterior crural does not differ from nerves to other portions of the quadriceps femoris.

Turning next to the origin of the sensory fibers within a muscle itself, Sherrington examined the muscle spindles, structures first seen by August Weismann in 1860, named by Willy Kühne in 1863, and tentatively identified as special sense organs by Angelo Ruffini in 1889. Combining a detailed study of the spindles' anatomy with his nerve degeneration and histological work, Sherrington showed that the structures (1) lie numerously embedded in the muscular tissue and are especially frequent in the vicinity of aponeuroses and tendons, and (2) function as end organs for the afferent fibers in muscular nerve trunks which end in the posterior spinal root ganglia.[29]

Sherrington's interest in muscle spindles was sharpened by his awareness of their physiological implications: the stimulus to which they are especially adapted, he pointed out, is *mechanical* in quality. In his knee jerk experiments he had found, first, that lengthening and increasing the longitudinal strain in a passive muscle by stretching it is a very efficient way to evoke discharge of impulses along its afferent nerve supply. Secondly, he discovered, contracting the muscle by electrical excitation of its motor filament only, even when the muscle lies loose from its attachment, also causes discharge of afferent impulses.[30] The structure of the muscle spindles, he realized at once, helped to provide a conception of how both modes of excitation may mechanically affect the endings of the sensory nerves in muscles.

During the 1920's Sherrington and Liddell's classic studies of the stretch reflex, using isometric myography and isolated knee extensor muscles, greatly clarified the role of sensory organs in muscles. The precise way in which the adequate stimuli for these organs becomes operative was revealed by other workers, using the sophisticated microtechniques of modern neurophysiology, near the end of Sherrington's life.

Sherrington's paper of 1894 paved the way for these later studies by establishing the existence of sensory fibers in and from muscles, and the presence in muscles of sensory organs responding to both stretch and contraction independently of sensations from the overlying skin. He had taken the first major step in experimentally supporting Longet's assertion that "the

first condition for harmony in muscle movement is the sensation of its accomplishment."

SENSORY PATHWAYS

Sherrington's paper on motor fibers of the lumbo-sacral plexus (1892) had largely resolved the nature of motor pathways from the anterior spinal roots to the limb muscles. At the suggestion of Dr. Rose Bradford, he had begun, around 1890, the parallel task of mapping sensory pathways from the skin to the posterior roots as another "step preliminary to some observations on the functions of the spinal cord." [31] His findings, published in two long papers of 1894 and 1898, provided maps of the cutaneous distribution of the thoracic and post-thoracic and of the cranio- and cervico-brachial posterior spinal roots, and confirmed his earlier conclusions about the significance of limb plexuses.

Prior to Sherrington's all-out assault there had been few studies, experimental, morphological, or clinical, of sensory root distribution. The experimental problems involved were one obvious reason for the scarcity: for example, an experimenter can only use observation and inference, for an animal cannot tell us what it feels. While some studies had been made with frogs and rabbits, Sherrington was the first to analyze the sensory distribution of cervical and brachial nerves in the monkey; Ludwig Türck (1810–1868) had made the only prior investigations of cutaneous fields in the mammalian (dog, human) hind limb.[32]

Sherrington's "mapping" methods. Sherrington's study of sensory innervations comprised a number of experimental series on the frog, cat, and monkey — the use of the monkey, a costly animal, made possible by the Royal Society's financial aid.[33] As we have observed before, much of Sherrington's success as a researcher must be attributed to his methodology, and a study of the procedures he used in mapping sensory pathways provides a fascinating glimpse of how he evolved his techniques.

The paper of 1894, treating spinal pairs below the brachial

plexus, was divided into five parts: preliminary observations on frogs, Experimental Series I A, B, C on cats and monkeys, and Series II on monkeys. In examining the distribution of the frog's seventh through tenth spinal nerves, Sherrington first tried cutting through a particular nerve root and testing the limb surface to find a corresponding area of anaesthesia. Recognizing, however, that the occurrence rather than the absence of muscular movement was a more reliable index of afferent nerve ties, he adopted Eckhard's technique of decerebrating the frog and dividing the nerve roots above and below the one under study — a technique named "the method of remaining anaesthesia" by the neurologist Henry Head in 1891.

After division of the nerve roots, the limits of the area from which a reflex movement could be elicited were determined as an index of the distribution of afferent nerve filaments. To elicit reflex movements Sherrington first used a rapid series of weak induction currents, and then switched to the more satisfactory methods of mechanical compression and bits of blotting paper soaked in weak sulphuric acid.

In Experimental Series I Sherrington again used the method of remaining anaesthesia for mapping sensory pathways in the limbs of cats and monkeys, and performed postmortem dissections to determine the segmental number of the individual roots. He paid special attention to the reflex to be used as a criterion for the existence of afferent fibers. The reflex, he noted, should be at least roughly quantifiable, not easily fatigued by repetition, not liable to be evoked by intrinsic nervous actions or extraneous events, and able to be clearly detected by a feeble stimulus. Seeking for such a reflex he tested and abandoned in turn arterial blood pressure, size of the pupil, and respiratory rhythm before selecting, as Eckhard had, the occurrence of local reflex muscular movement.

The second series of experiments were run to check out observations in Series I that were unexpected and not in harmony with data on the frog or with the scheme of distribution of efferent fibers in the lumbo-sacral plexus. To delimit the monkey's sensory root fields, Sherrington's basic method was that used for the frog, modified in the light of his subsequent ob-

servations in Series I. A particularly difficult problem was how to record most fruitfully and permanently his data on Macacus.

He first tried to keep a record of the skin fields by transferring their dimensions to proportional paper, but found himself "frustrated [in] this attempt" by differences of size and shape from monkey to monkey. Next he proposed to "content" himself with accurate measurements from comparatively fixed points and written descriptions illustrated with pencil sketches. This attempt too was abandoned for want of accuracy, and he moved on to record photographically the final stages of each experiment, using heavy double-line markings on the pigmented skin of Macacus to overcome the discovery that "for photography in winter in London the ink marks often did not show up sufficiently." Lastly, the location of skin points obtained were transferred to pre-made plaster casts of each subject, a technique that enabled Sherrington to build up models with patterns of the various root territories. "It was only when that had been done," Sherrington observed, "that certain important points in the scheme of their arrangement became salient." [34]

The methods for Series II, laborious as they were, proved to be extremely fruitful and were used by Sherrington in the second phase of his study of sensory pathways, the examination of cranio- and cervico-brachial posterior spinal roots. In addition to this task, Sherrington, with his customary penchant for thoroughness, "concurrently determined by separate experiments" the motor fields in the muscles of these regions, "in order to obtain a more perfect idea of the scheme of distribution of each entire spinal nerve." [35]

The results of his second comprehensive study of sensory pathways, published in the 1898 paper, fell into a number of categories. He depicted the general features of sensory innervation and gave detailed analyses of the shape and constitution of each sensory spinal skin field. In addition, by synthesizing the sensory innervation data with that from the motor pathways' research, he analyzed the segmental scheme of innervation of the limbs. Here, in sum, he showed how and why the field of distribution of motor and sensory spinal roots to the muscles and overlying skin of limb regions are widely different.

Thirdly, Sherrington presented his conception of the vertebrate limb's segmental architecture. During the latter half of the nineteenth century a prevailing view in comparative anatomy was that the vertebrate's body plan is that of a fore-and-aft series of fundamentally similar units. Sherrington, however, asserted that "it is altogether idle to look for exact homologies between the component parts of the brachial and pelvic limb." The ontogonies of the two limbs, he felt, are distinct, and any correspondence between them is similarity, not identity. Instead of trying to construct identity out of approximate resemblance, Sherrington suggested, anatomists should "note the fact that broad similarity of requirement and use has from broadly similar segmental material evolved, at two places of the ventro-lateral aspect of the quadruped, two separate structures so curiously alike, as are the brachial and pelvic limbs." [36]

THE PRELIMINARY STEP IS TAKEN

If one reads through the approximately 700 pages of Sherrington's publications from 1884 through 1898, he will appreciate why Sherrington found the anatomical researches laborious and frequently dull and pedestrian. But a reader will appreciate even more the quantitative and qualitative magnitude of those necessary "preliminary steps" which Sherrington took in pursuing knowledge of the reflex functions of the spinal cord. In the brief compass of this chapter we have dealt with some of Sherrington's methods and with his most general findings and conclusions, hoping thus to suggest the nature of the new paths he opened in anatomical and physiological knowledge.

To summarize the most important results of his anatomical studies: Sherrington found that (1) most muscles are multiply innervated and can be stimulated reflexly from different levels of the spinal cord; (2) each afferent spinal root contributes to several nerve trunks and thus produces overlapping of skin fields; (3) each afferent spinal root has a continuous and self-contained segmental skin field; (4) the segmental sensory supply of skin may differ greatly from the motor supply of underlying muscle; (5) the "formation of *functional* collections of nerve-

fibres [peripheral nerve-trunks] out of *morphological* collections [nerve-roots] . . . *is the explanation* — the meaning — of the existence of nerve-plexuses";[37] (6) sensory fibers exist both in and from muscles, and muscles possess sense organs functioning independently of the overlying skin.

Finally, in his 1897 Croonian Lecture on "Spinal Reflex Action," Sherrington presented a short summary table of spinal organization:

The spinal apparatus of the limb may . . . be likened to a funnel, the wide entrant mouth of which is represented by sensory nerves, the narrow end of exit by the spinal motor roots to the musculature. In the upper limb the sensori-motor funnel has the following segmental extension:[38]

		Cervical.						Thoracic.			
Number of spinal nerve —	II.	III.	IV.	V.	VI.	VII.	VIII.	I.	II.	III.	IV.	V.
which evokes reflex movement of limb		+	+	+	+	+	+	+	+	+	+†	
which supplies sense-endings in skin of limb			+	+	+	+	+	+	+	+		
which supplies motor innervation to muscle of limb				+	+	+	+	+	+			

and in the lower limb the following: —

	Thoracic.		Post-thoracic.									
Number of spinal nerve —	XI.	XII.	I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.	X.
which evokes reflex movement of limb		+	+	+	+	+	+	+	+	+	+	
which supplies sense-endings in skin of limb			+	+	+	+	+	+	+	+		
which supplies motor innervation in muscle of limb				+	+	+	+	+	+	+		

Here, simply and clearly given, was the anatomical foundation upon which Sherrington built the physiological structure of his integrative action concept.

IV

Reflex Functions: Problems and Methods

The mystery of nature needs no superstition.
— *Jean Fernel*

Concomitant with the anatomical researches that occupied most of Sherrington's time until 1898, and often deriving from them, came a profusion of ideas and observations on the reflex functions of the spinal cord. The two central, intertwined lines of these researches were the analyses of antagonistic muscle action and of larger "pieces" of reflex "machinery" such as the extension, flexion, and scratch reflexes of the hind limb. Out of these studies emerged Sherrington's conviction that the "main secret of nervous co-ordination . . . lies in the compounding of reflexes," [1] a compounding built up by the play of reflex arcs about their "common paths." Behind this play, in turn, lie the key processes of inhibitory and excitatory actions at the junctional regions between nerve cells — at the synapse.

In this chapter, as a background to understanding their fusion in the concept of integrative action, we will outline the development of ideas about antagonistic muscle action, inhibitory processes, and the concept of the synapse. Secondly, essential for understanding *how* Sherrington accomplished this fusion, we will examine some of the methods which he used to study the reflex functions of the spinal cord.

ANTAGONISTIC MUSCLE ACTION

"A striking feature of reflex organization," writes a contemporary neurophysiologist, "is the way in which facilitation and inhibition influence motoneurons reciprocally so that reflexly induced muscular contraction occurs without opposition." [2]

Ever since antiquity, biologists have realized that for animal movement to be coordinated and economical, opposing muscles must not work against each other. Recorded speculation about the functional interactions of antagonistic muscles began with

Galen, who introduced the view that when a muscle contracts its antagonist remains dormant.[3] In contrast to the Galenic idea, Descartes in his *De Homine* (1662) suggested that muscle antagonism involves an active process. When the eye's internal rectus muscle relaxes, he observed, the external rectus contracts and causes lateral rotation of the eye. To account for such a happening Descartes postulated a peripheral mechanism: the valved channels (nerves) that conduct animal spirits to the muscles are so arranged that the inflation of muscle "A" precludes inflation of "B," and at the same time permits the spirits of "B" to flow into "A."

In the eighteenth century, while Albrecht van Haller was championing Galen's thesis, yet a third view was introduced by J. B. Winslow. Antagonistic muscles, he suggested in his *Anatomical Exposition,* contract concurrently, the contraction of one muscle offering a "moderating resistance" to that of the other. Winslow's theory, as extended and modified in the following century, was a widely held one and led to vigorous and protracted debate over the functional relations between antagonistic muscles.

The idea that muscle antagonism is an active process received its first experimental support from Charles Bell. In 1823, describing an experiment in which flexor contraction coincided with imposed relaxation of the antagonistic extensor, Bell wrote the following striking anticipation of Sherrington's principle of reciprocal innervation: "The nerves have been considered so generally as instruments for stimulating the muscles, without thought of their acting in the opposite capacity, that some additional illustration may be necessary here. Through the nerves is established the connection between the muscles, not only that connection by which muscles combine to one effort, but also that relation between the classes of muscles by which the one relaxes and the other contracts." [4] Winslow's view, in turn, received its first extensive laboratory testing and support in the researches of H. Beaunis (1885, 1889) and Demeny (1890). Their work, in the main, showed that under normal conditions there is a simultaneous contraction of antagonistic muscles during *voluntary* movement.[5]

A new chapter in the investigation of antagonistic muscle action was opened in 1897, when Charles Sherrington told his audience at the Royal Society's Croonian Lecture: "My own observations lead me to believe that *inhibito-motor* spinal reflexes occur *quite habitually and concurrently* with many of the *excito-motor* . . . This co-ordination I term 'reciprocal innervation.' " With these words he explicitly linked antagonistic muscle action with the equally debated and little understood phenomenon of inhibition.[6]

THE NATURE OF INHIBITION

Behind Sherrington's first researches into the nature of inhibition as seen in reciprocal innervation lay half a century of growing speculation and experimentation on the phenomena of peripheral and central inhibition.[7] As is evident in the pages of Foster's and Landois and Stirling's texts, the second half of the nineteenth century saw an increasing awareness of the modifiability of reflex action and of the unitary functions of the nervous system. Prior to the concept of integrative action, investigation of these topics had begun to crystallize around the study of *central inhibition* and *facilitation* of reflex responses.

The first definite evidence for the suppression or inhibition of an organ's activity by stimulation of an appropriate nerve had come in 1845, with the classic demonstration by Eduard and Ernst Weber of cardiac arrest by vagal stimulation. In the next decades many such instances of the action of specifically inhibitory nerves were uncovered, such as Hering and Breuer's demonstration of the respiratory stretch reflex (1868), and Krönecker and Meltzer's discovery (1883) of the superior laryngeal nerve's inhibitory action in the swallowing reflex. But these types of inhibition, as Mary Brazier observed, "seemed simple to . . . physiologists faced with the complexities of inhibition in the central nervous system." Indeed, wrote one researcher in the 1880's, "of all the functions of the nervous system none is so mysterious in its nature or so obscure in its workings as that of inhibition." [8]

The possibility that inhibitory phenomena in reflex actions

have a central rather than a peripheral seat had been implicit from the time of Robert Whytt. He and numerous later workers had commented upon the ability of an individual to inhibit voluntarily certain reflexes such as sneezing, and had noted the increased activity of the spinal cord after removal of the brain. Equally prevalent, however, was the idea that the inhibition seen in a process such as muscle antagonism is a peripheral process — one occurring in the muscle itself rather than in the "nerve centers" of the brain or spinal cord.

The whole problem of reflex inhibition, as Sherrington pointed out in 1913, moved to the central nervous system because investigators failed to find specific inhibitory peripheral nerves for vertebrate skeletal muscle. "As a working physiological thesis," Sherrington wrote in 1900, the notion of central inhibition "only became accepted doctrine after Setchenov." [9]

In 1863 Johann Setchenov (1829–1905), a professor of physiology at Moscow University, published a monograph on inhibitory mechanisms controlling spinal reflexes in the frog.[10] Using Türck's method for measuring reflex time, Setchenov ran three series of experiments on various parts of the brain and brain stem, involving sectioning, chemical (salt crystal) and electric stimulation, and physiological tests. The data from these experiments confirmed his belief that the brain possesses "centers" inhibiting spinal reflexes and indicated that the centers are located in the optic thalamus, corpora quadrigemina, and medulla.

Setchenov's experiments, particularly those showing a great loss of reflex excitation when the optic lobes and thalami were treated with sodium chloride crystals, were cited widely as the conclusive demonstration of central inhibitory processes. There were, however, prompt and strident objections to his data and to the vast number of specific centers which his theory demanded. Alexander Herzen and Moritz Schiff, for example, repeated Setchenov's work and demonstrated that strong irritation of *any* part of the nervous system, central or peripheral, is accompanied by depression of reflex activity; they postulated that *each* spinal segment exerts an inhibitory influence on all posterior segments.[11]

The vast amount of experimentation stimulated by Setchenov's controversial "center theory" led to the formation of a number of competing ideas, which we may term the "interference," "metabolism," "drainage," and "inorganic salts" theories of central inhibition. It was against the background of these theories, and the emergence of the synapse concept, that Sherrington began to work out his ideas about the roles of central inhibitory and excitatory states in motor behavior, and about the reflex nature of inhibition itself.[12]

In his classic study of the spinal frog (1869), Goltz had proposed that a given activity of a reflex center is inhibited when the center receives any other afferent impulse.[13] This notion was expanded in the 1870's and 1880's by workers such as E. van Cyon, Lauder Brunton, and Charles Mercier, and was named the "interference theory" in 1902 by H. E. Hering. Holding that nerve conduction occurs in the form of a wave motion, they explained inhibition in terms of a wave interference phenomenon, a neutral process which leaves the tissue in the same condition as that in which it found it.

The interference theory was less crude than Setchenov's center theory and explained a greater number of phenomena, but it had a major fallacy that was recognized as early as 1880: the nerve impulse is not a truly undulatory phenomenon like the conduction of light or sound. Furthermore, as Sherrington pointed out, central inhibition is not a neutral process, for in many cases "it leaves the reflex centre surcharged for subsequent response." [14]

Another set of theories were those which related central inhibitory and excitatory events to metabolic processes. These metabolism theories were derived from Ewald Hering's famous theory of color sensation (1878), based on the opposing reactions of assimilation (anabolism) and dissimilation (catabolism).[15] As extended to neuromuscular action, inhibition was assumed to be associated with the assimilative phase of the nerve's metabolic cycle, during which there was a building up or recovery of energy and the nervous system was less sensitive to stimuli. Excitation, conversely, was held to occur during the dissimilative phase, with a discharge of energy. Gaskell, who built his me-

tabolism theory on a study of the cardiac nerves, wrote in an 1886 paper that "evidence is becoming stronger every day that every tissue is innervated by two sets of nerve fibres of opposite character . . . I look forward to the day when the whole nervous system is mapped out into two great districts with anabolic and katabolic functions to the peripheral tissue." [16]

The Hering-Gaskell theory was a focus of intense interest for nearly two decades, with research centering on the question of whether inhibition could be shown to be a product of the anabolic phase of the nerve cell's metabolism. The theory became generally discredited by about 1912 through failure to find this connection and recognition that the concept had been based on the faulty assumption that an increase in anabolism *necessarily* means a decrease in catabolism.[17]

A third major contender for the explanation of central inhibition was the "drainage theory," most fully formulated by William McDougall in 1903.[18] The theory, in essence, rested on the idea that nervous energy flows along nerve fibers as does liquid through a pipe, and may be drained off, dammed, or concentrated at particular points. Considering the nature of this drainage system in the central nervous system, especially in "higher processes" such as attention, McDougall concluded that inhibition in one part is always associated with excitation in another. On the basis of this view, he developed a model in which collateral neurones drain available "neurin" (nervous energy) from one neural chain into another strongly stimulated one. As a result of the drainage the first chain cannot function, causing inhibition of the muscle to which it leads. While McDougall's theory, too, failed to stand the test of experiment, it was for a time a fruitful source of studies in both physiology and psychology.

Although the precise nature of central excitation and inhibition remains uncertain today, neurophysiologists generally agree that the processes involve chemical transmitters at synaptic junctions. Sherrington was an early proponent of the chemical or neurohumoral theory, which grew out of the early twentieth-century researches of men such as Howell, MacCallum, Loewi, Cannon, and MacDonald.[19] Studying the role of inorganic salts

in nerve processes, J. S. MacDonald formulated a thesis that inhibition is caused by an immobilization of ion transfer. To him, the underlying conditions of rest and excitation in a nerve lay, respectively, in the physical attachment and partial detachment of inorganic salts to colloid proteins. "In an excited tissue," Sherrington said, summarizing MacDonald's idea, "an unusual quantity of inorganic salts is in motion. Excitation is ended by the reduction of this excessive motion. Inhibition is the condition in which the possibilities of free motion are most reduced."

Of all the preceding attempts to explain the nature of central inhibition, Sherrington in 1906 viewed MacDonald's as the most "fertile in suggestion for further experiment . . . The features and conditions of occurrence of inhibition harmonize strikingly with what on MacDonald's view we should expect them to be." [20]

THE SYNAPSE

"Nowhere in physiology," Charles Sherrington began his 1904 Silliman Lectures, "does the cell-theory reveal its presence more frequently in the very framework of the argument than at the present time in the study of nervous reactions." [21] These words reflected the growing impact of the neurone theory upon ideas about the central nervous system's structural and functional architecture at the turn of the century. Although the reticularists, led by Golgi, tenaciously clung to their views, many physiologists rapidly accepted the facts and imports of the theory Cajal had proposed in 1889. E. A. Schäfer, writing in 1893 on "The nerve cell considered as the basis of neurology," dismissed the reticular theory with the words, "it was formerly supposed that all nerve-cells were united with one another by distinct processes."[22] In its place he presented the following new "general conclusions":

(1) . . . every nerve-cell forms a structural element which is anatomically isolated from but in physiological continuity with other nerve-cells.
(2) . . . the physiological continuity . . . depends on the contiguity of ramified cell-processes of different nerve-cells with one

another, or of the ramified processes of one cell with the body of another cell. By this contiguity such isolated anatomical elements become concatenated into nerve-chains which may be either simple . . . as . . . possibly in the ordinary reflex chain of vertebrates, or may be complicated to any imaginable extent.

(3) . . . the same nerve-impulses do not necessarily pass from one element of a nerve-chain to the next, but . . . more probably new impulses . . . are generated in the successive elements of the chain.

As Schäfer's words suggest, many details in the neurone theory were uncertain, especially concerning the junctions between nerve cells: what are the exact anatomical boundaries between the cells, and how is their "physiological continuity" effected? [23] Understanding of these relationships began to emerge in 1897, when Hans Held announced his discovery of "Endfusse" ("end feet") and Sherrington introduced the term "synapse." From that time on, discussion of the "central machinery" controlling reflex functions began to be cast in the clearer terms of the neurone theory, of events at the synapse, rather than in the shadowy terms of "nerve centers" and "barriers of resistance."

Hans Held, the discoverer of the terminal branches of nerve processes, worked at Leipzig, where Wilhelm His had demonstrated the separateness of neuroblasts in embryonic tissue in 1886. Held, in contrast, studied nerve cells in adult tissue, and his discovery of "end feet" within this tissue ironically served to strengthen his adherence to the reticular hypothesis. As reported in his 1897 paper, Held observed that the axonal nerve endings were broken up into "neurosomes" — coarsely vacuolated and granulated protoplasm — which were protoplasmically continuous with the dendrites or the body of the adjacent cell. Terming the axonal endings "Endfusse," Held hypothesized that they were the zones for transfer of stimuli between nerve cells. But, he emphasized, this transfer takes place across a network of fine protoplasmic "concrescences," not by "contact." [24]

In the same year that Held announced his discovery of Endfusse within the "reticular network," Charles Sherrington, writing in the seventh edition of Foster's *Textbook of Physiology,* stated: "So far as our present knowledge goes we are led to think

that the tip of a twig of the [axon's] arborescence is not continuous with but merely in contact with the substance of the dendrite or cell body on which it impinges. Such a special connection of one nerve-cell with another might be called a synapsis." [25]

The circumstances behind Sherrington's introduction of "synapsis" were related by him in a letter to John Fulton on December 25, 1937:

M. Foster had asked me to get on with the Nervous System part (part iii) of a new edition of his 'Textb. of Physiol.' for him. I had begun it, and had not got far with it before I felt the need of some name to call the junction between nerve-cell and nerve-cell (because that place of junction now entered physiology as carrying functional importance). I wrote him of my difficulty, and my wish to introduce a specific name. I suggested using syndesm (σὐνζεσνος). He consulted his Trinity friend Verrall, the Euripidean scholar, about it, and Verrall suggested "synapse" (from συγἀπτω-αγω), and as the yields a better adjectival form, it was adopted for the book.

The concept at root of the need for a specific term was that, as was becoming clear, 'conduction' which transmitted the 'impulse' *along* the nerve-fibre could not — as such — obtain at the *junction,* because a 'membrane' there lay across the path, and 'conduction' per se was not competent to negotiate a 'cross-wise' membrane . . .

'Synapsis' strictly means a *process* of contact — i.e. a proceeding or *act* of contact, rather than a *thing* which enables contact i.e. an *instrument* of contact. 'Syndesm' would not have had that defect, i.e. it would have meant a 'bond.' [26]

The significance of Sherrington's opting for the neurone rather than the reticular theory and his coining of "synapsis" has been clearly stated by Granit. "When Sherrington decided in favor of nerve-cell contacts he refashioned thinking in this field along lines that determined its future course for all time and also tied it to the newly born science of electrophysiology . . . Only a contact theory could bridge the gap between reflex transmission and electrophysiology; such is the power of a fundamental concept like the synapse." [27]

The work of Leopold Auerbach (1857–1936) in 1898 suggested that Held's Endfusse could be the points of transfer for nerve impulses across zones of contact or "synapsis," rather than across continuous protoplasmic threads. While Auerbach did

not deny the existence of "nodes" in a "reticular network," he did report that his silver chromate method showed the end feet of at least some cells to be separated from each other by a definite hair-line boundary. The nature of the contact between these apparently discrete cells, Auerbach noted, is obscure, but there is no evidence of a special "Zwischensubstanz" uniting the Endfusse.[28]

That Endfusse *do* exist in large numbers on both axons and dendrites, and that there *is* a definite membrane separating the Endfusse of contiguous nerve cells, was dramatically revealed between 1903 and 1904 by Cajal's reduced silver nitrate method.[29] Exactly *how* nerve impulses are transmitted across the junction between end feet, Cajal admitted in his 1906 Nobel Prize address, is a perplexing question. Perhaps, he and others suggested, there is an induction or "action at a distance," or perhaps the transmission is effected through a granular cement or a special conducting substance uniting the neuronal surfaces.

Neurophysiologists are still unraveling the nature of synaptic transmission. But, as Sherrington indicated in his letter to Fulton, workers in the 1890's quickly grasped the fact that this process, whatever its nature, had enormous significance. Schäfer, for example, noted in his 1893 article that the events at the "adjunctions" between nerve cells in a reflex arc might aid in explaining the phenomenon of reflex time: "Physiologically it may be shown that there is always a partial block to the passage of a nervous impulse at the conjunction of one cell with another . . . This lost time which occurs at the junction of the cell-chain represents the period of latent excitation of the nerve-cell." Sherrington, writing on the problem of reflex time in Schäfer's *Text Book of Physiology,* similarly observed that "it is not improbable that the relative number of these [synaptic] blocks will furnish a key to the differences which are found to obtain in the reaction time for different reflexes." [30]

Sherrington felt that other central nervous system phenomena, too, might be explained by the properties of the synapse. For example, he suggested, the one-way conduction in a reflex arc may be due to the valve-like behavior of the synapse rather than to the "dynamically polarized" conduction within a nerve cell

from dendrite to axon described by Cajal.[31] Ideas about synaptic properties and their relation to reflex phenomena were explored, in detail and upon an experimental basis, in the Silliman Lectures. The "characters distinguishing reflex-arc conduction from nerve-trunk conduction," Sherrington demonstrated, "may be largely due to intercellular barriers, delicate transverse membranes, in the former." [32]

"TECHNIK IST ALLES"

An ideal method for any scientific experiment is that which allows only one factor at a time to vary. The central nervous system, as any student of physiology soon discovers, seems expressly "designed" to baffle such an approach because of its complexity and the ways in which it is influenced by virtually every external and internal stimulus impinging upon it.

The barrage of claims and counterclaims regarding the reflex functions of the brain and spinal cord during the nineteenth century clearly derived, in large measure, from an inadequate base of anatomical knowledge combined with haphazard and imprecise physiological methods. Sherrington, like other nineteenth-century investigators of the anatomy, histology, and physiology of the nervous system, was thus confronted with the task of devising techniques for reducing and controlling the nervous system's structural and functional complexity to the point where meaningful data could be obtained.

His first steps, we have seen, were (1) to concentrate upon the reflex functions of the spinal cord rather than the more complex field of the brain; (2) to choose an appropriate experimental animal, the monkey, and run parallel experiments on a variety of lower forms for controls and comparisons; (3) to establish the necessary points of anatomical knowledge on which to rest functional studies.

A complex of additional factors further combined to make Sherrington's neurophysiological researches so manifestly successful. Many of his techniques, skills, and work habits were developed and sharpened in the course of his anatomical studies: operative procedures, means of stimulus standardization,

ways to exclude extraneous variables from experiments, methods of recording data, and the thorough testing of any hypothesis, however laborious and monotonous the labor involved.[33]

In contrast to today's sophisticated microtechniques and physicochemical ways of analyzing biological phenomena, Sherrington's basic method was to study simple motor acts which could be made to occur in isolation, such as antagonistic muscle actions and, on a more complex level, the simple and compound reflexes of the hind limb. An integral part of this method was to correlate the exacting analyses of the input-output relations of reflex responses with anatomical and histological data. The combination of physiological, anatomical, and histological data, Sherrington felt strongly, was essential for a knowledge of function. And, as he constantly advised his students and practiced himself, these tripartite labors should all be done by the researcher. "One of the striking things about Sherrington's scientific career," John Fulton noted in his diary, "has been the intensely personal nature of all his investigations; if he is going to count the fibres in a nerve, he dissects out the nerve itself, and prepares it, stains it, and sections it by his own hands, and counts the fibres himself thru his own microscope. He is rather scornful of the people who have a dozen assistants running around making sections and doing counts, *etc.* 'How can they possibly know that it is correct?' " [34]

To study simple acts of muscle management at the spinal level in the living animal, Sherrington eliminated the higher controlling regions of the brain and brain stem. He reduced his experimental animal to a functioning, isolated spinal cord or cord segment, able to execute limb reflexes in response to given stimuli. Approaching still closer to the ideal of one variable at a time, he could further simplify these simple reflexes by isolating single muscles and their nerve pathways.

Analyzing the simple reflex contractions of muscles in vivo and comparing them to phenomena such as the twitch of an isolated nerve-muscle preparation and conduction in a peripheral nerve trunk, Sherrington gradually unveiled the characteristic properties of reflex pathways through the spinal cord. By then studying the interplay of these pathways in successively

larger and more complex reflexes, he slowly built up a picture of the pattern of integrated motor behavior in an intact, normal animal.

In sum, as Sherrington expressed it in dualistic terms, he reduced his experimental animal to the state of a Cartesian "puppet-animal," in which "the mindless body reacts with the fatality of a multiple penny-in-the-slot machine to certain [physical] stimuli . . . A point is that these mindless acts yet treat the animal's motor machinery as a united whole. Thus the mindless machine can walk, and run, and gallop; it can also spring . . . There is integration although purely motor integration." [35]

The puppet animals. Sherrington's "puppets" were of two types: the classic "spinal animal" whose cord has been permanently transected above the lumbo-sacral enlargement, and the "decerebrate animal." [36] Decerebration, by actual removal of the cerebrum or by transection of the brain stem, was an old technique, and its effects had been described by many earlier workers, including Magendie, Longet, Flourens, and Bernard. To Sherrington, however, must go the credit for having named *decerebrate rigidity* and demonstrated its importance both as a phenomenon in its own right and as a major tool for examining the reflex functions of the spinal cord, particularly the nature of inhibition and reciprocal innervation. As depicted in Sherrington's classic description of 1898, the decerebrate animal assumes the characteristic posture which he termed decerebrate rigidity: knee and elbow joints stiffly extended, tail stiff and straight, head retracted, and chin thrown upward.[37]

Sherrington's successful use of decerebrate mammalian preparations was due primarily to the exacting methods and insights which characterized his work. Decerebration is a fairly easy operation in birds, and had been performed often since the 1820's when Pierre Flourens published his classic researches on the decerebrate pigeon. In mammals, however, bleeding often compresses the respiratory center and, if decerebration is incomplete, the animal makes powerful limb movements. Both factors are probably responsible for the fact that so few early observers

of decerebrate animals reported the extensor rigidity. Sherrington succeeded, as no one had previously, in observing the rigidity and discovering that it is a persistent condition, lasting up to four days, by attending to such seemingly small details as checking hemorrhage by ligating the carotids and temporarily compressing the vertebrals until a clot formed.[38]

In spite of operative problems, the use of decerebrate preparations for neurophysiological research had been advocated in the 1860's by such eminent figures as the Parisian professor of anatomy and pathology, E. F. A. Vulpian. The decerebrate animal, unless stimulated by the experimenter, remains quietly at rest — "an animal," as Flourens said of his pigeon, "condemned to perpetual sleep" — making it vastly preferable to an animal quieted by the uncertain and volatile anaesthetics of the day. H. Sanders-Ezn, in 1868, had used a decerebrate frog, with the cord cut in the lower thoracic region, to study the role of motor roots in reflex responses. Following Sanders-Ezn's method, Sherrington's use of a decerebrate mammal with the cord transected and anaesthesia then remitted provided him with an ideal experimental preparation: an isolated length of spinal cord, with a good blood supply free of anaesthesia, in which he could analyze reflex paths at will.[39]

Sherrington probably used a decerebrate monkey to study spinal reflexes as early as November 1894, and during the summer and fall of 1896 he began to explore more fully the effects of decerebration. The first fruits of his study appeared in January 1897, when he published a description of "Cateleptoid reflexes in the monkey." These reflexes, Sherrington wrote, were of "extremely prolonged duration, and absolutely devoid of clonic character and of alternating character," quite in contrast to the reflexes usually elicited from the isolated cord. "Not [their] least interesting part," he promptly realized, "is a remarkable glimpse which they allow into the scope of reflex inhibition as regards the co-ordinate movement of the limbs." [40]

Moving on toward his classic definition of decerebrate rigidity, Sherrington described the effects of transecting the neural axis at the level of the crura cerebri in the cat in a second paper of January 1897. The animal, he reported, shows "tonic"

or "extensor" rigidity with no tremor or marked relaxations in certain groups of skeletal muscles, "especially those of the dorsal aspect of the neck and tail and of the extensor surface of the limb." He used the terms "decerebrate rigidity" and "decerebrate tonus" to describe this condition in his Croonian Lecture in April 1897.[41]

Ever since Sherrington's fundamental paper of 1898, the origin of decerebrate rigidity has been a challenging question. Sherrington's main interest in the decerebrate animal was as an experimental tool, chiefly for examining the play of central inhibition and excitation, and he thus explored its causes only as necessary to ensure its fruitful applications.[42]

Decerebrate rigidity as seen in the monkey and lower animals, Sherrington observed, is due immediately to prolonged spasms of certain groups of muscles, chiefly the retractors of the head and neck, elevator and dorsal flexors of the tail, and extensors of the elbow, knee, shoulder, and hip. Seeking the factors initiating and controlling these prolonged spasms, he first decided that since the condition persists indefinitely it cannot result from irritations incidental to the trauma of decerebration.

Working from this basic decision, he pinpointed various regions of the spinal tracts and motor cortex whose stimulation or sectioning variously caused an increase, abolition, or temporary inhibition of the contraction of the muscles. A particularly significant finding occurred when Sherrington studied the effects of ablating one cerebral hemisphere: homonymous extensor rigidity appeared, and subsequently often totally subsided and reappeared several times. There seemed to be, he judged, "a struggle between two conflicting influences, as though a tonic influence from the still intact crossed hemisphere at times overcame and at times was overcome by another opposed influence from a lower centre." [43]

Defining the nature of this "lower centre" influence was perhaps the most significant phase of Sherrington's first studies of decerebrate rigidity. Studying the effects of cutting posterior nerve roots and of stimulating various peripheral nerves, he demonstrated that decerebrate rigidity is a spinal reflex, excited and maintained by "a set of reflex reactions which employ the

local deep afferents (proprioceptive) and some cranial mechanism seated between the cerebrum and bulb." [44]

From his work on hemiplegia, the British neurologist John Hughlings Jackson (1835–1911) formulated the concept of *release of function* in 1884: destructive lesions in the higher brain centers produce "negative" conditions allowing "positive" signs and symptoms to appear at lower levels.[45] Sherrington's study of decerebrate rigidity, showing that it must be viewed as a "release" of the lower brain stem and cord from the inhibitory control normally exercised by the forebrain, gave experimental proof of Jackson's principle. With the work of Henry Head, release of function became a fundamental neurological principle.[46] Thus Sherrington's "puppet animal" was a major element, both conceptually and technically, for deciphering the reflex functions of the spinal cord and the levels of control operative in the central nervous system.

V

Reciprocal Innervation (1893–1900)

In the simple correlation uniting antagonistic muscle-pairs, inhibition of antagonist accompanies excitation of protagonist . . . In all cases inhibition is an integral element in the consolidation of the animal mechanism to a unity. It and excitation together compose a chord in the harmony of the healthy working organism.[1]

In the preceding chapters we have dealt with a complex of factors that helped to shape Sherrington's analysis of spinal reflex actions: the nature of structural and functional knowledge and the problems engaging neurophysiologists as he began his work, the emergence of the neurone theory, his own analyses of sensory and motor pathways, and the techniques and procedures which he used in his work.

The most important theme in Sherrington's functional researches up to 1900, both for his understanding of the operations of spinal reflex per se and for his comprehension of the mechanisms of nervous coordination, was his analysis of antagonistic muscle action. For it was the principle of reciprocal innervation, as Lord Adrian has commented, "which opened the way to the further advance from the simple to the complex. It was the clue to the whole system of traffic control in the spinal cord and throughout the central pathways." [2]

THE KNEE JERK AND ANTAGONISTIC MUSCLE ACTION

The results of Sherrington's exhaustive analysis of reciprocal innervation are found chiefly in his fourteen classic "Notes" published in the *Proceedings of the Royal Society* from 1893 through 1909.[3] The first "Note," "On the correlation of action of antagonistic muscles," stemmed from observations he had made on the knee jerk while studying the motor fibers of the lumbo-sacral plexus.

Sectioning the afferent or efferent spinal roots either just above or just below the root on which the jerk depends, he discovered, exalted the jerk by abolishing the hamstring muscles'

tonus. Sherrington then asked himself whether the loss of tonus increased the jerk in a purely mechanical fashion, or if the exaltation was a physiological phenomenon. A series of experiments on factors causing abolition or enhancement of the jerk favored the second alternative. The jerk's exaggeration, he reported in his first "Note," seemed due to "interrupting a stream of centripetal impulses that passes up from the hamstring muscle and enters the spinal cord by certain afferent roots, and in the cord exerts a depressing or restraining influence on the jerk." [4]

The work reported in this "Note" provided the first sound experimental support of Erb's thesis that the knee jerk is a reflex phenomenon. Sherrington had shown, in essence, that the jerk can be inhibited centrally as can other spinal reflexes. The debate over the knee jerk, however, was far from settled, for supporters of the "idiomuscular theory" continued to raise the issue of reflex time, and argued too that Sherrington had not directly inhibited the jerk but had inhibited the mysterious "tonus" of the muscles on which the jerk is dependent.[5]

Each of Sherrington's experiments on a specific problem tended to produce a host of other issues that engaged his attention — a fact which accounts for the profusion of data and ideas crowding the pages of his papers. The manner in which his knee jerk studies led him into an analysis of antagonistic muscle action typifies this aspect of his work.

Data reported in the first "Note" suggested that antagonistic muscle action, and the inhibitory processes it involves, is an *active* and *central* phenomenon.[6] For in the case of the knee jerk, at least, Sherrington had found that excitation "of the afferent fibres from one set of the antagonistic muscles induces reflex tonic contraction of the opposing set with extreme facility, despite the fact that the opponent muscles are not innervated from the same spinal segment." [7] It was "obvious" to Sherrington that this correlation of action between the thigh and knee antagonists, involving central excitation and inhibition, might "be not widely different from the type of peripheral excitatory and inhibitory processes originally pointed out by Hering and Breuer [1868] as regulative of the movements of respiration." But, he realized, much more work was needed before a com-

parison between central and peripheral inhibition could be drawn in detail.[8]

His second "Note" continued to examine the "qualities of alteration restraining or abolishing the jerk," adding evidence for its being a reflex dependent on a central spinal mechanism. And, his work on the knee jerk muscles having suggested a search for instances of analogous correlation, he reported the results of his first experiments on antagonistic muscle action in the eye muscles and palpebral (eyelid) apparatus.[9]

Sherrington chose to study the "delicately correlated muscles of the eyeball" because even slight alterations in their length are readily apparent. In the 1870's Ferrier had discovered that stimulation of a given area of the motor cortex causes conjugate movement of both eyeballs in a direction away from the hemisphere stimulated. Using the cat and monkey, and examining the correlation between the internal and external recti muscles, Sherrington sought to discover how this conjugate movement is executed. After paralyzing the internal rectus, he found that excitation of the left or right motor cortex still produced conjugate movement of both eyeballs to the side opposite the cortical point stimulated. But the movement of the left eyeball was "never seen quite so rapid or so ample as that of the right eye." Thus, he concluded, the conjugate movement appears to be caused by *active contraction* of the left internal and right external recti and *concurrent inhibition* of the tonus of their antagonists (the left external and right internal recti).

On the basis of experiments such as the foregoing, and earlier ones showing that the cortex can inhibit the action of striated muscle, Sherrington began to analyze the levels of control operative in antagonistic muscle action. His results, he felt, supported the "widely accepted doctrine" that the cerebrum "nominally exerts a more or less tonic inhibitory influence over the lower local centres subserving muscular tonicity and local muscular reflex action." [10] Another experiment seemed to require the assumption that the cortex can inhibit *active contraction* as well as tonus in skeletal muscle:

> If, after section of both right and left 3rd and right and left 4th cranial nerves, the left frontal cortex be excited and both eyes

made to deviate to the right, excitation of the right cortex . . . will not infrequently cause the right eye to move inwards and sometimes fully up to the primary position. The active contraction of the external rectus appears to be cut short and even converted into a condition of relaxation more complete than when no cortical excitation at all is being employed.[11]

RECIPROCAL INNERVATION DEFINED

Apart from an 1894 paper dealing further with eye muscle antagonism, the bulk of Sherrington's publications from 1894 through 1896 dealt with his anatomical researches. He returned to the analysis of antagonistic muscle action in 1897, which was the most productive year of his life in terms of number of publications: he wrote sixteen original papers.

The term *reciprocal innervation* was first used in the title of Sherrington's third "Note," read before the Royal Society on January 21, 1897. The term, he explained in the "Note," denoted the "particular form of correlation" in which one muscle of an antagonistic couple is relaxed as its mechanical opponent actively contracts. Four months later, as the Royal Society's Croonian Lecturer, he proposed his classic definition of reciprocal innervation as that form of coordination in which "inhibito-motor spinal reflexes occur quite habitually and concurrently with many of the excito-motor." [12]

From 1897 through 1900, as reported in the third through sixth "Notes" and in other papers, Sherrington continued to analyze the nature of reciprocal innervation and to extend demonstrations of the range of its occurrence. By the turn of the century he had firmly established reciprocal innervation as a widely occurring phenomenon, showing that it may be produced by excitation of skin and peripheral nerves, the dorsal spinal column, the anterior surface of the cerebellum, and the crura cerebri, pyramidal tract, internal capsule, optic radiations, Rolandic cortex, and occipital cortex.

Concerning the mode of operation of reciprocal innervation, Sherrington's first studies had shown that the process must be viewed as an active and central one. As for the levels of nervous system control, he reported in his third "Note," it is not *es-*

sential that the "high level" centers be active for the type of "elementary co-ordination" effected by reciprocal innervation.

Sherrington's work clearly showed that reciprocal innervation enables the isolated spinal cord of the spinal or decerebrate animal to execute simple coordinated limb movements. He had found too, however, that reciprocal innervation can be induced by stimulating "higher levels" such as the pyramidal fibers in the crura, and that it occurs in willed movements such as those of antagonistic eye muscles.[13] Accordingly, he pointed out in the third "Note," in the normal animal "this kind of [reciprocal] co-ordination at elbow and knee is probably largely made use of in movements initiated *via* the cerebral hemispheres as well as in the lower reflexes." [14]

We have seen how Sherrington's researches on the existence of sensory nerves in muscles aided him in identifying decerebrate rigidity as a spinal reflex. His study of "muscular sensibility" again bore fruit when he examined the operation of reciprocal innervation at the spinal level. Applying his knowledge that a reflex may be elicited by a purely muscular reaction, he showed in 1899 that electrical stimulation of the central cut end of an exclusively muscular nerve (that of the hamstring) inhibits the tonus of its antagonist (the knee extensor muscles). Moreover, he found, the same effect is produced when the flexors are exposed and detached from the knee, making them mechanically incapable of affecting the position of the joint, and then are stretched or kneaded. Such data, he reasoned, show that "reciprocal innervation may be secured by a simple reflex mechanism, an important factor in its execution being the tendency for the action of a muscle to produce its own inhibition reflexly by mechanical stimulation of the sensory apparatus in its antagonist." [15]

The role of muscular sensibility in reciprocal innervation was further explored in the sixth "Note." [16] As any observer can discover, spinal reflexes are characterized by a "machine-like regularity and fatality of movement," yet similar stimuli may elicit different and even opposite reactions in a spinal animal. Sherrington felt that these variations in response are due primarily to differences obtaining in the spinal organ itself,

and his observations of hind limb reflexes in the spinal frog suggested that one determining factor is the limb's posture when a stimulus is applied. He noted, for example, that when the animal's initial posture was extension at hip, knee, and ankle, stimulation of any part of the limb excited flexion as the primary reflex movement. Conversely, when the initial posture was flexion, stimulating the skin within a small gluteal area generally produced extension at the hip joint.

The fact that the extension response occurred when all the skin had been removed from the hind legs ruled out the nerves of the limb's cutaneous sense organs as the mechanism controlling the influence of posture on reciprocal innervation. Thus, Sherrington decided, the postural effect may be referable to "afferent nerves subserving the muscular sense, and connected with sense-organs in the muscles, tendons, and joints."

By 1900 Sherrington's researches had thus revealed a great deal about the nature of antagonistic muscle action. He had found it to be a widely occurring phenomenon, active rather than passive in its operation, brought into play through a central rather than a peripheral mechanism, dependent on the integrity of afferent nerves from muscles, and at the spinal level involving the reciprocal processes of inhibition and excitation.

Of fundamental importance for his understanding of the principles of muscle management, he had shown reciprocal innervation to be a basic element in motor coordination. "Reflexes obtained from the decerebrate animal," he wrote in 1898, "exhibit . . . 'reciprocal innervation' . . . in such distribution and sequence as to couple diagonal limbs in harmonious movements of similar direction." [17]

In view of the ways in which Sherrington's definition of the mode and role of antagonistic muscle action reshaped understanding of nervous system activity, the following words from his Croonian Lecture must rank, in retrospect, as a classic understatement in the annals of neurophysiology: "In short, my observations prove the existence of 'reciprocal innervation' of antagonistic muscles as part of the machinery of spinal reflexes,

and point to it as possibly a widely extensive part of that machinery." [18]

REFLEX MUSCLE MANAGEMENT

With reciprocal innervation as the key reflex phenomenon revealing patterns of "traffic control" in the central nervous system, Sherrington had begun by 1900 to form a comprehensive picture of the motor functions of the spinal cord. His conception of these functions, of the "rules" which govern them, and of their role in the unitary functioning of the nervous system were developed between 1897 and 1900 in his Croonian and Marshall Hall Lectures and in the pages of E. A. Schäfer's *Text Book of Physiology.*

The organism and its segments. "The individual," Sherrington told his Marshall Hall Lecture audience on May 23, 1899, "is a mass of living units, their activity co-ordinated together by conductive strands (nerve cells) reacting to the environment." The sense organs — olfactory, gustatory, visual, auditory, cutaneous, muscular, and visceral — serve as the "channels of access" in this interaction between the organism and its environment.[19]

As for the physiological analysis of the nerve cells in the spinal system, Sherrington affirmed in 1900 that "the unit reached is the 'reflex.' Upon it as a basis our existing notion of the reaction of the nervous system is built." As his anatomical work had shown, the "edifice" of the nervous system, whose functional unit is the reflex, is based, as upon two pillars, upon two nerve-cells": the afferent and the efferent root-cell, each possessing cutaneous, muscular, and visceral branches. These two root-cells, he stated, "form a fundamental spinal arch upon which all other neural arcs are superposed and functionally rest . . . even those of the hemispheral cortex." [20]

Sherrington, in broad terms, viewed the nervous system as consisting of two great "segments," the head and the body. Through the course of evolution, as he explained his conception in the Marshall Hall Lecture, the "head pole" of the

vertebrate body has become, "so to say, the individual." At the head pole are located the "great projicient senses" of sight, smell, hearing, and stereotropism, and it is in this segment of the nervous system that the brain develops.[21]

Behind the head extends the animal's body: an elongated "motor mechanism" which drives the "lead pole" forward into visual space. The motor mechanism is endowed with lateral appendages providing mechanical leverage for the motor elements, a certain amount of visceral cavity, skin and its sense organs, and its own muscular sense.[22] It is this bodily apparatus, Sherrington explained,

> which chiefly executes the movements of the organism as a whole. It can alter the space relations of the mouth and sense organs in regard to the environment and thus facilitate the nutrition of the organism by securing food; it can remove the individual from situations of danger or injury. It is at the command not only of the sense organs resident in itself and its own covering, but also of the great sense organs near the head pole . . . and the motor organ itself is after all in the main their instrument.

Consonant with the above arrangement, he continued, strands of nerve conductors pass from the head pole to the contractile masses which form the motor organ. These conductile fibers are contained in the spinal cord, and in this sense the cord is merely an appendage of the brain. But the cord, Sherrington observed, also may be considered as an independent structure, for "the motor organ itself is a complex structure, built up of many parts. These, if the movements asked for by the projecting senses are to be adequately executed, must be co-ordinate in action." [23]

Sherrington's anatomical researches necessitated revision of the traditional nineteenth-century view of the spinal cord as a chain of functional segments. The fact of an anatomically segmental arrangement of the spinal nerves, as his mapping work had shown, carries no proof of a corresponding functional segmentation. The traditional "block" delimitation of the vertebrate spinal segment, he stated firmly in the Croonian Lecture, "is no longer defensible or useful." Thus in Sherrington's hands the term "spinal segment" was given a new *func-*

tional definition, designating the neurones of the posterior root ganglion and the corresponding anterior root, and all other intraspinal neurones whose cell bodies lie between the same frontal levels of a given efferent root.[24]

The "purpose" of the motor organ. By 1899 Sherrington's study of the play of antagonistic muscles in the spinal and decerebrate animal had shown beyond doubt that a main function of the spinal cord is the "regulation of the activities of the several muscles, so that they act co-ordinately."[25] Co-ordinate reflex movement, as workers had long observed, is *purposive* in character, but the interpretation of that "purposiveness" was highly controversial.

At the time when Sherrington worked, investigators had two frameworks within which they could cast discussion of reflex purposiveness: the evolutionary theory formulated in Darwin's *Origin of the Species* (1859), and the more metaphysically oriented doctrine of "spinal function," made famous through the continuous lively debate begun by Eduard Pflüger and Rudolph Lotze in the 1850's.[26] To Sherrington evolutionary theory offered the best explanation of the purposiveness evident in reflex phenomena. In light of the Darwinian theory, he believed, the normal connections between any afferent path and its motor apparatus "*can* only be such as to lead to 'purposive' movement," in the sense of having an adaptive or survival value for the organism.[27]

Spinal reflexes, Sherrington held, "unmistakably signify" three major types of purpose. First, preservation of the animal's sensorial surface, as seen in the grooming movements of the scratch reflex and the conjunctival reflex closure of the eye. Second, movements of progression: in the intact animal, he noted, spinal-level reflex movements contribute "chiefly toward preparatory posture in readiness for onset of action executed by the musculature under the driving of the higher centres." Third, the maintenance of visceral functions: if the bulb, cord, and their peripheral nerves are isolated from the rest of the nervous system, the animal "as regards its visceral life, including that of the heart and lungs, is practically intact."

Beyond starting that the motor organ exhibits these three types of "purposive actions," he asserted that "the whole ground of 'purpose' is speculative." [28]

"Rules" of spinal reflex action. For analyzing the purposes and mechanisms of spinal reflexes Sherrington had at hand the myographic records of his mapping work with Macacus. These records, he emphasized in appraising their usefulness, "possess points of interest, but it must not be forgotten that the value of a reflex obtained by exciting the afferent spinal roots . . . is slight as regards the light thrown by it on the normal workings of the cord." [29] Because the spinal root is a morphological rather than a functional unit, Sherrington perceived, an analysis of spinal reflex action must collate several sets of data: the morphology of the spinal roots and the reflexes obtainable from the roots, peripheral nerves, and skin-spots.

Pooling and analyzing these four sets of data, Sherrington formulated a series of "rules" observable in spinal reflex action.[30] For analytic purposes he divided the reflex apparatus of the cord into five regions, each composed of right and left halves: tail, pelvic limb, trunk, brachial limb, and neck. In terms of these divisions he found that spinal reflexes fall into two broad classes: *a short spinal reflex* is one in which the muscular response occurs in the same region as the stimulus, while in a *long spinal reflex* a stimulus applied in one region evokes a response in another region.

Examining the "irradiation" or spread of impulses in *long* intraspinal paths, Sherrington found and meticulously catalogued the numerous exceptions to the four "laws of reflex action" proposed by Eduard Pflüger in 1853. These "so-called laws," he wrote in an unusually critical tone, "have been so generally accepted as to have obtained a doctrinal importance which they really hardly merit." Indeed, he continued, it is more profitable to describe briefly the main features of long reflexes as seen in an experiment on the spinal animal than "to attempt adopting Pflüger's 'laws' so as to make them fit observed facts." [31]

Studying long reflexes in the spinal animal, Sherrington was

struck first by the fact that there were eight skin areas — the soles, palms, pinnae, tail, and cloaca — from which the reflexes could readily be stimulated. On the whole he discovered that the long reflexes evoked by stimulating these areas were "more variable and less certain and validly predictable than the short [reflexes]." Facility of spread from one lateral half of the cord to the other, for example, was very dissimilar at different cord levels. And in any given experimental series the long reflexes varied "in order of relative facility of direction of irradiation," and in "the sense of the movement elicited at the joint to which the irradiation extends." The difficulty of analyzing long reflexes, finally, was further compounded by the fact that "a region to which the reflex action usually demonstrably irradiates [often] was altogether omitted . . . throughout the whole of a lengthy experiment." [32]

Turning to the more certain field of study presented by the *short spinal reflexes,* Sherrington formulated five "rules" concerning their irradiation. The enunciation of the rules, he observed in Schäfer's *Text Book,* greatly aided in understanding the "machinery for working sentient surfaces"; moreover, he hoped, they may "incidentally cast light" upon the general physiology of the nerve.[33]

(1) Rule of segmental proximity: Concerning the amount of correspondence between the morphological structure and the functional mechanisms of the spinal cord, Sherrington found that "the degree of reflex spinal intimacy between segments is directly proportional to their segmental proximity."

(2) The above rule, he discovered, has a "logical corollary": "taken generally, for each afferent root there exists in its own spinal segment a reflex motor path of as little resistance as open to it anywhere [in the spinal cord]."

(3) Rule of pluri-segmental reflex arcs of low resistance: In response to an even approximately minimal stimulus of a single afferent root or root filament, Sherrington's excitation studies had shown that "the spinal discharge of centrifugal impulses evoked, tends to occur via more than one efferent root, i.e., is pluri-segmental." Corollary to this rule, as he had discovered in analyzing motor fibers in the lumbo-sacral plexus, particular

fractional combinations of several motor roots are the functional units in spinal reflex action. The movement produced by direct excitation of a *whole* motor root, he emphasized repeatedly, does not represent a functional movement of high coordination.

Since the motor discharge in each anatomical spinal segment is fractional, Sherrington reasoned, certain neurones will be selected and certain neglected with a given stimulus. This selectivity, he showed, explains the fact that some limb movements are easily provoked by spinal reflex action, while others are elicitable only rarely and with difficulty.[34]

In this pluri-segmental and fractional discharge arrangement, Sherrington realized, it is significant that not all the muscle groups about one joint are inaccessible and those about another joint accessible to short afferent paths. Instead, the difference in ease of accessibility occurs between antagonistic groups acting about one and the same joint. Thus, he saw, it is the pluri-segmental character of the motor nucleus, as expressed by reciprocal innervation, which gives the limb its functional solidarity — a perception of major significance for the genesis of the integrative action concept.

(4) Following from his definition of rule 3 and its corollaries, Sherrington enunciated the nature of reciprocal innervation in short spinal reflexes.

> The groups of motor neurones which in one and the same spinal segment exhibit marked inequality of local reflex excitability innervate antergetic muscles.
> The groups of motor nerve cells contemporaneously discharged by spinal reflex action innervate synergic and not antergic actions.[35]

He perceived that these two principles, plus the facts of pluri-segmental and fractional discharge, underlie and help to explain three aspects of coordinated limb movements: (1) certain movements about a single joint are opposed to each other; (2) certain movements about one joint are opposed to certain movements at another; and (3) when the motor groups of synergic muscles are synchronously activated they effect a harmonious movement of the whole limb, such as drawing it up and forward by cooperative flexions at the hip, knee, ankle,

and digits. Thus, he concluded, the synchronously acting muscle groups "can be considered to constitute one large functionally-connected nucleus, which itself may constitute an entity in the co-ordination of the limb in the movements of the body taken as a whole."

(5) Finally, following "almost as a corollary" from rules 1 and 4, Sherrington formulated the rule of uniformity of response: "Spinal reflex movements elicitable in and from any one spinal region will exhibit much uniformity despite considerable variety of the locus of incidence of the spinal stimulus." [36]

Sherrington's "rules of spinal reflex action" were forged from his knowledge of sensory and motor pathways and of antagonistic muscle action. They were rules, he stated repeatedly, which did much to explain the fact of coordinated muscle management at the spinal level. With this perception, as summarized in one brief sentence from the Croonian Lecture, we see him moving steadily toward the concept of integrative action: "In this way reflex action, by its 'spread' develops a combined movement, synthesizes a harmony." [37]

Levels of control. In the normal animal, as Sherrington had said in the Marshall Hall Lecture, the nervous system functions as a unity, with the "motor mechanism" both subservient to and acting upon the higher level centers of the brain. Accordingly, besides examining how motor reflexes "synthesize a harmony" of movement in the spinal animal, he was concerned with how they operate in the intact animal.

For Sherrington, in his work up to the turn of the century, a major clue to understanding levels of control in the nervous system came from the phenomenon of *spinal shock*. Students of reflex action had long recognized the occurrence of shock, which was first named and clearly described by Marshall Hall in 1850: "If we take a frog and divide the spinal marrow near the cranium, the animal is affected by *shock;* the diastaltic force is suspended, there are no diastaltic actions, or only such as are very feeble. In a few minutes the diastaltic power and phenomena are restored, the effect having passed away." Because shock is one of the major problems encountered in experimental or

natural injury of the nervous system, its nature and the mechanisms of recovery from it have attracted attention since Hall's time.[38]

Throughout the nineteenth century frogs and other cold-blooded animals were used most often for reflex studies because, as Hall had said, they soon recover from the effects of shock. In contrast, as the work of Goltz and his pupils with dogs had shown, spinal mammals may take hours, days, or even months to recover enough from shock to execute even weak reflexes.

Goltz was one of the few workers prior to Sherrington who had explicitly directed his attention to the nature of spinal shock. Sherrington judged his descriptions of shock as "masterly," but limited by the fact that they referred only to the dog and to transections below the middle of the back. Within these limits, Goltz classified all "temporary" paralyses following injuries to the brain or cord as *Hemmungserscheinungen.* These "inhibition-phenomena," he held, collectively comprise the phenomenon of "shock," which he believed was a long lasting irritation due to trauma.[39]

On the basis of his work with Macacus, Sherrington was led to challenge the prevailing interpretation of shock given by Goltz. The differences in response to cord severance between the dog and cat and the monkey and man, Sherrington pointed out in 1896, emphasize the dangers of too ready an extrapolation of findings between lower and higher forms. In the dog, cat, and monkey, he reported, the knee jerk persists for a few minutes after cord section. To him, this persistence indicated that the condition of the central part of the reflex arc, upon which the jerk's integrity depends, is not immediately altered by being cut off from the cerebrum. But in man, cord section immediately abolishes the jerk, showing that the cerebral component of spinal tonus is disproportionately greater than is the spinal component. Studying recovery from shock, Sherrington observed that the dog's and cat's knee jerk shows a lasting local spinal exaltation within one hour, the monkey takes at least one week to recover, and man shows a permanent depression.[40]

The observations above contain two related points; neither were original with Sherrington, but in his hands they became

important elements in understanding the nature and levels of control of muscle management. They were, first, the fact that after recovery from shock, reflexes below the transection become stronger or more easily elicited than they were before the transection — an example of the "release of function" which he applied in explaining decerebrate rigidity; and second, the fact that as one ascends the evolutionary series from frog to man, the effects of shock become increasingly severe and long lasting. Calling attention to this second point in his Croonian Lecture, Sherrington observed that "there can hardly be witnessed a more striking phenomenon in the whole physiology of the nervous system" than the initial shock due to spinal transection in the monkey.

> From the limp limbs, even if the knee-jerk be elicitable, no responsive movement, beyond perhaps a feeble tremulous adduction or bending of the thumb or hallux, can be evoked even by the insults of a character severe in the extreme. That which the delicate yellow spot is to the sensifacient sheet of the retinae, may the thumb and index be said to constitute in the great sensifacient field of the limb. Nevertheless, a hot iron laid right across the thumb, index, and palm, remains an absolutely impotent excitant; the crushing of the finger has no greater effect . . . A more impassable condition of block, or torpor, can hardly be imagined.[41]

Another dramatic demonstration of the depth and severity of shock in higher forms was "paraplegia," a condition Sherrington met with in only some monkeys and never in the dog. The paraplegia, he found, may not set in until as much as forty-five minutes after transection below the brachial plexus, when "with cold hands and ears the animal lies down listless, and perhaps unconscious, with respiratory movements of the Cheyne-Stokes type. This state may persist twelve hours or so, and end either in gradual recovery or death." If recovery did occur, the animal's reflex actions were and remained "feeble and poverty stricken," in striking contrast to the vigorous reflex movements soon obtained after the dog or cat has recovered from shock.[42]

To encounter so great a physiological contrast between the effects of shock in mammalian types, Sherrington felt, was "surprising." The dog seemed to differ less from the frog than

did Macacus from the dog, although the morphological gap is much greater between the former than the latter pairs. Further thought and study, however, indicated that although the contrast is "great and significant" it is not "really profound," for it is quantitative rather than qualitative. The difference between the variety and extent of reflexes elicitable from the spinal monkey and from the cat or dog, for example, was greatly reduced when the spinal roots were stimulated near their ganglia instead of stimulating the skin and nerve trunk. From findings such as this Sherrington concluded that the "spinal machinery" for movement is actually present in the monkey, as it is in the dog or cat, but is "more difficult to set in motion and keep going" because of the severity of shock.[43]

In sum, Sherrington found following prolonged observation that the effects of spinal transection in the monkey proved to be permanent: a *true deficiency phenomenon* or *Ausfallserscheinungen,* not the *Hemmungserscheinungen* of Goltz's theory. The whole difference between his and Goltz's view of shock, he admitted,

> is as far as not merely a matter of nomenclature, a question on which no definite decision seems as yet possible. I myself have gradually been driven to the belief that 'shock' does not take long to pass off, i.e., does not at longest persist for more than a few days . . . Much of what is called 'shock,' in regard to the Mammalian cord is, I believe, due to 'isolation-alteration,' and is really permanent . . . The most favourable time for the examination of the independent capabilities of the spinal cord is that when the sum of 'shock' and 'isolation-alteration' together is of the smallest amount.[44]

Although the nature of shock was debatable and its causes not precisely known, his study of it aided Sherrington in understanding the interrelations between the brain and the spinal cord in vertebrate motor behavior. Near the end of his Marshall Hall Lecture, he stated:

> I think it was Lotze who said that doubtless to the trodden worm, of these two halves the trodden 'me' shall surely appear the greater. By a high spinal transection the splendid motor machinery of the vertebrate is practically as a whole and at one stroke severed from all the universe except that fraction of the 'material me.' The

deeper depression of reaction into which the higher animal . . . sinks when made 'spinal' appears to me significant of this, that in the higher types, more than in the lower, the great projecting senses actuate the motor organ, and impel the motions of the individual. That deeper depression shows how, as the individual ascends the scale of being, the more . . . cognizant does it become of the circumambient universe outside that is 'not me;' and thus the latter acquires a more and more preponderant directive influence over those reflections, those expressions of the creature's neural states, its 'doings.' [45]

MECHANISMS OF CONTROL: MUSCULAR SENSIBILITY, "HEMMUNG," "BAHNUNG."

Until the conjunction of the neurone theory and Sherrington's analysis of spinal reflexes, the mechanisms effecting the coordinated movements of a normal animal (an "untrodden worm") generally were depicted in the vague terms of the "nerve network" and "barriers of resistance." Between the network of cerebro-spinal connections open to afferent paths, it was supposed, there are "barriers of resistance" so graded and adjusted that only synergic motor units are excited, and these only to the degree necessary for a given movement.

In terms of this view, Sherrington reflected in 1900,

it might have been supposed that with the cerebro-spinal organ maimed by subtraction from it of the entire brain, any afferent path entering the central nervous system, and there connected with . . . potentially all the motor spinal units, would . . . act on the motor units so indiscriminately as to induce, if strongly stimulated, complete discharge of all of them, or, if weakly stimulated, feeble or incomplete discharge of all of them. Such discharges would of course produce unnatural movements.[46]

In reality, as observers of spinal animals had long known, if the "motor organ" recovers from shock it is perfectly capable of executing purposeful and coordinated movement.

Prior to Sherrington's work four interacting factors had been isolated as the chief determinants of purposeful, coordinated spinal reflex movements: the character of the afferent impulse, stimulus intensity, stimulus locus, and the intrinsic condition of the spinal cord. Sherrington subsequently showed that at a

gross functional level the movements are effected by the reciprocal innervation of antagonistic muscles. By 1900 he had pinpointed three key mechanisms which in turn effect and affect the operations of reciprocal innervation: the muscular sense and the processes of central inhibition and facilitation.

The fact that the organism can function without the guidance of its "head pole" indicated to Sherrington, first, "that some set of spinal sense organs forms the chief basis of the mechanism ensuring such elemental co-ordination." The cutaneous sense organs had been ruled out by his demonstration that coordination is preserved in skinned spinal animals. And it seemed to him "hardly possible that the co-ordination is to so large an extent an innate quality of the motor unit groups themselves." Accordingly, in a conclusion well supported by his anatomical and physiological data, Sherrington designated the sense organs in the "musculo-articular apparatus" as the basic mechanism of muscle management by the cord or cord segment.[47]

Although guided by information from these sense organs, the isolated cord needs additional means to prevent a discord of movement. These means, Sherrington saw, were provided by the fact that "reflex arcs, both higher and lower, are inter-connected. The condition of one is partly dependent on the condition of many others." As many investigators had pointed out by 1900, the effect of this interdependence may take two forms: the depression of local reflex reactions — "Hemmung" or "inhibition" — or the promotion of a local reflex reaction — "Bahnung" or "facilitation." [48]

Although central inhibitory and facilitatory processes were recognized by the turn of the century, their causes, as we saw in Chapter IV, were a subject of controversy. Sherrington was less concerned, however, with the basic causes of inhibition and facilitation than with their roles in motor coordination. In view of the widespread occurrence of antagonistic muscle action in the body, action which involves reciprocal processes of inhibition and excitation, Sherrington judged that "it is probable that inhibition of one spinal 'centre' by another plays a great part in the elementary co-ordination of actions executed under spinal mechanisms." [49]

It was equally evident to him that facilitation plays an important role in harmonizing the spread of impulses throughout the spinal cord. He noted, for example, that spinal reflexes frequently show phenomena analogous to the "staircase contractions" seen in cardiac and skeletal muscle. If, he wrote, one excites an afferent root with a stimulus of given strength, and returns to it after having excited reflexes from a neighboring root, "the strength of the stimulus required has fallen to considerably lower than it had been originally, and this happens under circumstances which seem to preclude any other changes in the conditions than the intercurrent stimulation of an adjacent root." [50]

Sherrington was aware that there were no bases in the physiological or physicochemical knowledge of 1900 to substantiate any given theory of the processes underlying inhibition or facilitation. Thus, in Schäfer's *Text Book,* he was content simply to present a brief summary of their *possible* mode of operation in reciprocal innervation.

> The incitement to activity of functional group A of motor units seems colligate with inhibition of the functional group B, whose muscles are antagonistic to those innervated by A. By what mechanism this is ensured is not clear. Group A may have a path not only to the muscles but to the nerve cells of group B, by which it can depress the activity of the latter. Or each spinal path that embouches into A may also embouch mediately or immediately into B, and while exciting A inhibit B. This latter does not necessarily imply two different kinds of disturbance in the paths opening upon A and B respectively; a difference between the condition obtaining at the moment in A and B motor units may determine a different reaction in them under an external influence which falls similarly on both. Whatever the detailed explanation, it is certain that co-ordination is a character common to all reflex actions from the unpoisoned spinal cord, and that reciprocal innervation largely expresses that co-ordination.[51]

From the vantage point of retrospect the historian can see that by 1900 Sherrington had assembled the major ingredients of the concept of integrative action. Proceeding from his knowledge of sensory and motor paths and the existence of the "musculo-articular" sense organs and nerves, he had applied

his basic, exacting "input-output" analysis to a host of reflex phenomena. From a study of the seemingly simple anatomy and physiology of the knee jerk he had become engaged with a series of broader problems, such as the nature and mechanisms of antagonistic muscle action, the production and maintenance of decerebrate rigidity, and the nature of spinal shock.

Out of the mountains of data collected in the course of these researches Sherrington developed a number of basic functional principles: reciprocal innervation, interaction between higher and lower level centers of motor control, and the muscular sense, inhibition, and facilitation as three key mechanisms of muscle management at the spinal level. And, recognizing the import of the neurone theory for his work, he had perceived that many of the characteristic properties of reflex pathways might, at root, be explicable by the events at the synapse.

By the time Sherrington sat down to write on the spinal cord in Schäfer's *Text Book,* these facts and principles clearly had begun to coalesce in his mind. From his discussion of the "influence of associated parts on the central organ" flashes the basic perception of integrative action: to say that "the nervous system is a unity" is to say that "each even local reflex action is in truth a reaction to all sensifacient stimuli incident on the individual at the moment in *sum* both as to space and as to time. And those activities of the central nervous system which are customarily spoken of as autochthonous, have also, on account of the inter-connection of the arc, influence upon the reactions of other arcs. The influence arising either way may take expression in . . . inhibition [or] facilitation." [52]

Taking the final steps from this perception to the full-grown integrative action concept, Sherrington determined how interdependent reflex arcs combine to form successively larger and more complex reflex patterns, such as those of the scratch reflex.

VI

The Scratch Reflex Paradigm

Today . . . experiment begins at last to make, as Euripides wished, things talk and tell men what they are.

— *Jean Fernel*

At the turn of the century, moving toward an understanding of the whole pattern of reflex muscular control in the intact animal, Sherrington began to study larger and more complex reflex actions than the "elementary co-ordinations" effected by reciprocal innervation. This second phase of his functional researches evolved around the *scratch reflex* of the spinal dog.

The operation of the scratch reflex, engaging many more muscles than does a relatively simple reflex such as the knee jerk, confirmed his earlier observations and theses: the same functional principles, he found, obtain in both the simple and most complex reflex actions. And, because of its very complexity, the scratch reflex further illuminated a wide range of central nervous system phenomena underlying motor coordination, such as inhibition, facilitation, summation, spinal induction, and the events at the synapse.

THE SCRATCH REFLEX: FIRST OBSERVATIONS

Sherrington began to study the scratch reflex while extending the analysis of short and long reflex paths first made in his Croonian Lecture. Specifically, he had continued to accumulate evidence for the "numerous and wide departures" from the fourth "so-called 'law' " of Pflüger — that in associated spinal reflex centers irradiation spreads more easily toward than away from the head.

In 1902 he and E. E. Laslett reported on the microscopic course of "descending intrinsic spinal tracts." For their study they developed a lengthy but highly fruitful variant of the Wallerian method, which they termed the *method of successive degeneration*. With it they soundly contravened Pflüger's fourth

"law" at an anatomical level, showing that abundant *aborally*-running fiber systems, long and short, originate from the posterior cervical, mid- and post-thoracic, and anterior lumbar spinal segments.[1] They continued their demolition of Pflüger's "law" on a physiological level in a paper of 1903, in which they showed that four long reflexes in the dog employ aborally-running spinal paths.[2] One of the four, reflex scratching, must have been recognized for centuries — particularly by any dog owner — but it had received scant attention in experimental literature until Sherrington turned to it.

Earlier workers occasionally had described as "quasi-scratch" the movements of the decerebrate frog's foot in wiping away acid-soaked bits of paper from its flank. H. Munk and Goltz mentioned observing true reflex scratching in monkeys and dogs after cortical excisions and lesions, and Goltz and his pupil Freusberg had given a general albeit vague description of the dog's scratch reflex. In the English literature an equally slim contribution had been made in 1889 by J. B. Haycraft, who noted that reflex scratchings "are sometimes present, sometimes absent, in animals nearly related." This variation, he judged, "depends no doubt on the habits, and build, of the animal itself." In the dog, he observed somewhat obviously, the "sensory area from which this reflex may be initiated . . . includes those parts of the skin to which the hindfoot can be approximated." [3]

As described far more rigorously by Sherrington and Laslett in 1903, the spinal dog's scratch reflex can be elicited by rubbing or scratching a skin-field which includes the hind part of the back of the neck, a zone around the front of the chest, the axillary fold over the triceps, and the loin and flank. The reflex, they noted, consists of a rapidly alternating flexion and extension at the knee and ankle and the hip, usually beginning with plantar flexion of the digits so that the foot becomes claw shaped, and with flexion and protraction at the hip.

Cataloguing the reflex's properties, they observed first that it is "enormously exaggerated, vigorous, and facile," continuing with unaltered frequency up to three and one-half minutes after stimulus cessation.[4] The frequency of its rhythm, they found, is

affected by stimulus strength but little if at all by stimulus frequency. Stimulus locus also affects the reflex, for the scratching paw is carried further forward when the stimulus is placed further forward.

On the basis of physiological tests, Sherrington and Laslett felt that the reflex pathways involved in scratching are uncrossed. With bilateral stimulation the reflex movements remained unilateral but shifted sides from time to time, indicating that the reflex of the crossed side was regularly cut off by the stimulus that evoked the crossed reflex. Analyzing these alternating movements, Sherrington again saw the mechanisms of antagonistic muscle action and the muscular sense at work in spinal reflexes.

Part of the scratch reflex's apparatus, he decided, must be some maintained posturing of the crossed hind limb which either inhibits a scratching movement or prevents access to it of the effective stimulus. He and Laslett further found that the reflex continued to be self-supporting if the limb was placed so that in scratching it did not touch another part of the body, or any other object. This observation, coupled with the fact that the reflex was rapidly stilled by "gently confining" limb movement, indicated that the alternating scratching movement was being maintained reflexly by mechanical stimulation of the afferent nerves of the muscles and joints involved.

Concerning the reflex's long intraspinal paths, Sherrington and Laslett found that the afferent neurones which initiate the scratching run from the cervico-thoracic field to the lumbosacral motor neurones via an uncrossed descending path in the lateral column. Accordingly, they pointed out, the skin-fields, spinal segments, and conduction lines of the scratch reflex are vast, embracing afferent pathways from III-V Cervical to II-XIII Thoracic, and motor neurones scattered from at least II Lumbar to I Sacral. Yet, as Sherrington's anatomical work had shown, there are long mononeuronic fibers linking the cervical and sacral segments. On this basis, he and Laslett stated, it is possible that the scratch and other long reflexes, especially in their uncrossed portions, need only a *trineuronic* (disynaptic)

arc, composed of an afferent root cell, a long spinal neurone, and an efferent root cell.[5]

In another paper of 1903, analyzing the nature of stimuli evoking the scratch and direct extension reflexes, Sherrington defined an important new principle concerning the *stimulus locus.* Physiologists generally had distinguished among qualitative differences in spinal reflexes provoked from the skin only as far as they depended on differences in the regional locus of their initiation. Sherrington's mapping of sensory spinal skin-fields, however, had shown the variety of types of sensations elicitable from the skin. This variety suggested to him the possibility that different reflex motor reactions are connected with different species of end-organs "undoubtedly co-existing in one and the same skin-field." [6]

If the skin underneath and between the toe-pads and cushion of the spinal dog's hind foot is pressed or stretched there is a sudden, forcible extension of the limb — the direct extension reflex. Such a movement, Sherrington perceived, is helpful in contributing to progression, but obviously would be harmful if it occurred in response to certain other foot stimuli. And indeed, he found, pricking rather than pressing the toe-pad causes flexion instead of extension, showing that in the undersurface of the hind foot two qualitatively different stimuli evoke two polar reflexes. This fact, he thought, might be explained by one of two hypotheses: (1) two different sets of afferent nerves are directly connected with two opposing elements of the limb's motor mechanism; or (2) the two afferent nerve sets are connected with both flexors and extensors, but one set acts primarily in an excitatory manner on extensor neurones and in an inhibitory manner on flexors, or vice versa.

In a second set of experiments Sherrington showed that over a large skin area the hair and the nocicipient nerve endings of the skin surface are physiologically distinguished from pure cold and warmth endings and from all the deep cutaneous end-organs. This distinction was seen in the fact that the hair and nocicipient end-organs are spinally connected with the limb musculature so that their stimulation elicited a movement of

grooming the skin and its hairy coat — the scratch reflex.

In sum, Sherrington concluded, the different kinds of end-organs belonging to the same skin region "possess spinal reflex connections differing *inter se*." Recognition of this fact, he pointed out with full awareness of its import, provided physiologists with a new way to distinguish between end-organs: by characteristics given in the tension of the musculature, as well as by the standard sensory discrimination tests.

Sherrington continued his definition of the effective stimuli for the scratch reflex, and the mechanisms of its motor response, in a short paper "On certain spinal reflex in the dog" (1904).[7] The muscular contractions of the reflex, he observed, have a tonic as well as a clonic or rhythmic component, and the tonic element becomes more pronounced the more the stimulus is posterior and nearer to the mid-dorsal line. The reflex arc maintaining these tonic/clonic components, he said again, is disynaptic, with the first synapse in the same spinal segment as the stimulus locus and the second in the spinal segment innervating the limb's flexor muscles.

In further cataloguing factors affecting the reflex he noted (1) that its rhythm is modified considerably by internal conditions such as local fatigue and shock; (2) that it exhibits well the latent summation of subliminal stimuli, although once in progress stimulus rate has little effect on its rhythm; and (3) that it reveals numerous instances of inhibition: for example, by stimuli that excite prolonged tonic reflex flexion or by stimuli causing relaxation of the flexors of the scratching side.

Turning to the reflex's motor mechanism, Sherrington found that when scratching was in progress stimulation of a second skin spot modified elements such as its intensity and residual tonicity. But the second stimulus did not interfere with the rhythm of the clonic scratching elicited from the first skin spot. From these findings he argued (1) that the whole of the motor nucleus is occupied by the reflex in each case, and (2) that grades of reflex response intensity are due to grades of intensity of reaction by the individual constituent units of the motor nucleus, not to various fractions of the total number of component units.

THE PRINCIPLE OF THE COMMON PATH

By 1904, from investigations of reflex actions ranging from the relatively simple knee jerk to the more complex patterns of hind limb reflexes such as scratching, Sherrington had forged the detailed and comprehensive picture of reflex motor behavior which he presented as Yale's Silliman Lecturer in April 1904. In the same year he enunciated the nucleus of the integrative action concept in a presidential address to the Physiological Section of the British Association for the Advancement of Science. Published in the *British Association Reports* on August 18, 1904, "The correlation of reflexes and the principle of the common path" stands as Sherrington's most important *published* conceptual statement before *The Integrative Action of the Nervous System* (1906).

The physiology of the nervous system, Sherrington began in his address, may be studied from three main viewpoints: (1) the life of the individual nerve cell, (2) the specific functional property of nerve cells — conductivity, and (3) the *integrative function* of the nervous system: how, by nerve cell conductivity, "the separate units of an animal body are welded into a single whole, and from a mere collection of organs there is constructed an individual animal." [8]

In studying integrative neural function, he continued, two main types of systems can be distinguished by the mode of union of the conductors: the *nerve-net system,* such as that seen in the coelenterate medusa and in the walls of viscera, and the *synaptic system* seen in the cerebrospinal apparatus of Arthropods and vertebrates. The functional units of the synaptic system considered in its integrative aspects, he proposed, are reflexes, whose chain of conduction consists of a *nervous arc* running from a receptor to an effector organ. The unit structures of the reflex chain, in turn, are *neurones,* so linked together that conduction along the chain seems possible in only one direction. This irreversible conductivity, he suggested as he had in 1900, is "probably referrable to [the] synapses," and "especially distinguishes the synaptic nervous system from the nerve-net system." [9]

Having given his audience the basic units and terminology of vertebrate reflex action, Sherrington turned to the main theme of his address: an analysis of the reflex chain of the synaptic system, in which he introduced his "principle of the common path." He pointed out first that a reflex chain's receptive neurone forms a *private path* into the brain or spinal cord, a path which is "exclusive for a single receptive point." When the receptive neurone passes into the "great central organ" it forms numerous connections with a vast network of conductive paths. Yet, as physiologists had recognized for some time, irradiation normally is limited to certain lines. "This canalisation of the network in certain directions from each entrant point is sometimes expressed, borrowing electrical terminology, by saying that the conductive network from any given point offers less resistance along certain circuits than along others . . . The pattern of arrangement of the conductive network of the central organ reveals something of the integrative function of the nervous system. It tells us what organs work together in time." [10]

Unraveling the conductive patterns of the central nervous system, Sherrington held, "stands high among the neurological advances of our time." But, he cautioned, "we must not be blind to its limitations," for the present schema of central nervous system patterns takes no account of temporal data. Temporal data, he stressed, *must* be considered in studying integrative functions, for the conductive pattern of the nervous system is not really immutable. "As a tap to a kaleidoscope, so a new stimulus that strikes the central organ causes it to assume a partially new pattern. The pattern in general remains, but locally the patterns are in constant flux of back and forward change." [11]

Within this complex, locally fluctuating conductive network, Sherrington explained next, many private paths may converge at an *internuncial neurone* to form a second type of reflex pathway: *a public or common path.* Internuncial common paths, in turn, run to the third link in the reflex chain, the *motor neurone.* From the motor neurone, finally, the impulses travel over a *final common path* to converge upon the effector organ. The

motor nerve to a limb muscle is one such collection of final common paths.

Sherrington saw that certain consequences flow from this arrangement of the reflex chain into private, public, and final common paths — consequences which in part explain how the interaction of reflexes effects motor coordination. The existence of public and final common paths, for example, seems to preclude "qualitative differences between nerve-impulses arising in different afferent nerves." For, Sherrington noted, "if two conductors have a tract in common there can hardly be a qualitative difference between their modes of conduction." [12]

A second outcome of the reflex chain's arrangement, of major importance in producing reflex correlation, is the fact that receptors using an effector for different purposes can only use a final common path *successively*, not simultaneously. "In my experience," Sherrington said, "when two stimuli are applied simultaneously which would evoke reflex action that employ the same final common path in different ways . . . one reflex appears without the other. The result is this reflex [such as flexion] or that reflex [such as extension], but not the two together." [13]

The scratch reflex, Sherrington told the members of the Physiological Section, is an excellent example of how the paths of the reflex chain interact to produce reflex correlation (Fig. 6). Considering the basis of the coordinated movements of reflex scratching, Sherrington explained first that various types of spinal reflex arcs may play upon the final common path of the reflex (from the motor neurone to the hip flexors). Secondly, he emphasized the fact that the nature of the correlation between these arcs — whether they are in *cooperation* or *competition* — may effect the enchancement, depression, or inhibition of the scratching.

He had found as one instance of cooperation that two subliminal stimuli applied to receptive points S_α and S_β (Fig. 6) in the dorsal skin fields reinforced each other, and through this facilitation evoked reflex scratching.[14] In terms of the scratch reflex's neural connections, the mutual reinforcement occurred because private paths S_α and S_β came into a public path relationship and

then simultaneously passed through the final common path to the hip flexor. "Such mutual reinforcement," Sherrington had found, "is usual between reflexes of identical species evoked from one and the same receptive field." [15]

In contrast, he reported, arcs within separate categories usually are so correlated in their action on the final common path as to antagonize one another. He had seen such rivalry for possession of the final common path when the skin of the hind foot was stimulated during reflex scratching: the scratching stopped and the foot was drawn up by a strong tonic contraction of the ankle, knee, and hip flexors. In terms of the primacy of purposive reflexes, he reasoned, the grooming reflex was displaced by a *prepotent* withdrawal-from-danger reflex. Such displace-

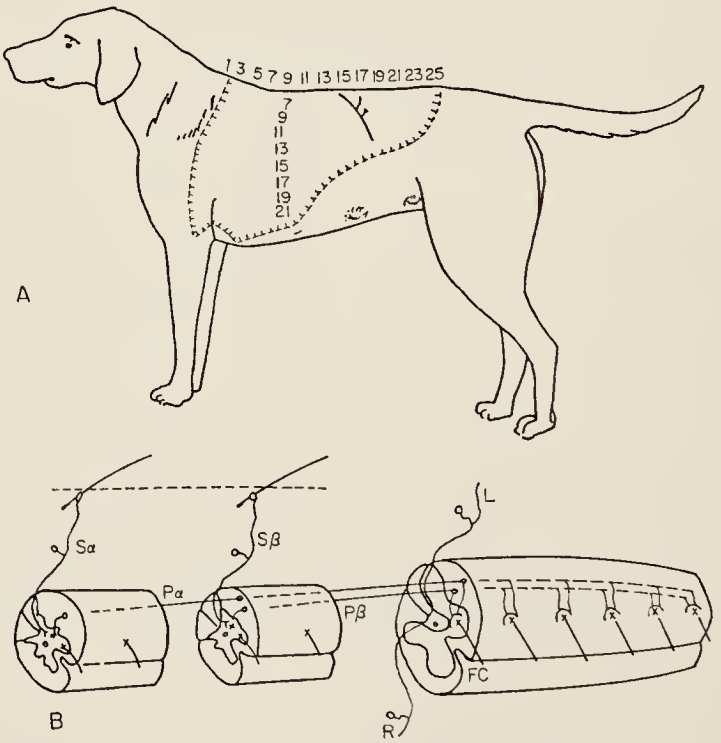

Fig. 6. *The Scratch Reflex.* (*A*) The "receptive field," as revealed after low cervical transection, a saddle-shaped area of dorsal skin, whence the scratch reflex of the left hind limb can be evoked. *lr* marks the position of the last rib. (*B*) Diagram of the spinal arcs involved. *L*, receptive or afferent nerve-path from the left foot; *R*, receptive nerve-path from the opposite foot; *Sα*, *Sβ*, receptive nerve-paths from hairs in the dorsal skin of the left side; *FC*, the final common path, in this case the motor neurone to a flexor muscle of the hip; *Pα*, *Pβ*, proprio-spinal neurones.

ment could occur, he explained via his diagram of the scratch reflex, because nociceptive arc *L* from the foot to the spinal segment runs into the same final common path as arc *S*, and thus can displace the scratch reflex from the final common path. When the nociceptive stimulus ceased, reflex scratching resumed, thus showing that "although there is no enforced inactivity, there is inhibition. There is interference between the two reflexes, and the one is inhibited by the other. Though there is no cessation of activity in the motor neurone, one form of activity that was being impressed upon it is cut out and another takes its place." [16]

With the above observations and analysis Sherrington had mapped a fairly complex reflex action, explaining its occurrence in terms of play of competing reflex arcs about a common path. The seat of this competition between the rival flexor and extensor arcs, he surmised, seems to lie not in the motor nerve but in the gray matter, where the arcs impinge together on the motor neurone. "That is equivalent to saying that the essential seat of the phenomenon is the *synapse* [between] the motor neurone and the axone-terminals of the penultimate neurones that converge upon it. There some of these arcs drive the final path into one kind of action, others drive it into a different kind of action, and others again preclude it from being activated by the rest." [17]

Sherrington realized that the extent of competition for use of a final common path is enormous. Histological counts, for example, had shown that the number of afferent fibers entering the human spinal cord is at least three times as great as the number of efferent fibers leaving it. While he urged that reflex arc competition and the converse process of mutual reinforcement take place at the synaptic fields of the motor neurones, he had to admit, in 1904, that "as to the nature of the physiological processes involved little, it appears to me, can be said." He could state, however, that three factors chiefly determine which arc will temporarily dominate a final common path: (1) the relative stimulus intensity of the rival reflexes, (2) the functional species of the reflex, and (3) fatigue, the waning of a reflex under prolonged stimulation. The phenomenon of fatigue, he

held, also occurs at the synapse and seems to be "a process elaborated and preserved in the selective evolution of the neural machinery . . . [to help] insure serial variety of reaction." [18]

Summarizing his conception of the common path and its role in the integrative functions of the nervous system, Sherrington likened the central organ (brain and cord) to a telephone exchange, where connections between starting and end points are changed from moment to moment to suit passing requirements. To realize the "exchange" at work, he suggested, one must see it as a combination of spatial plan and temporal data, whose incoming paths offer connections with varying degrees of resistance. These resistances are affected absolutely and relatively by the functional conductive activity of the nervous organ at a given moment, and by such general conditions as blood supply and nutrition.

Physiologists, Sherrington noted, commonly speak of an effector organ as being innervated by a given nerve. It would be "more correct as well as more luminous," he felt, "to speak of it as innervated by certain receptors; thus, the hip-flexor, now by this piece of skin, now by that, by its own foot, by the opposite fore-foot, by the labyrinth, by its own muscle-spindles, by the eye, by the 'motor' cortex, *etc.*" For it is temporal variability, he had perceived, which provides the synaptic system with a mechanism for higher integration, synthesizing an individual animal from a "mere collection of tissues and organs." [19]

"Expressed teleologically," said Sherrington, the common path thus is a coordinating device which "although economically subservient for various purposes, is yet used for only one purpose at a time . . . In this way the motor paths at any moment accord in a united pattern for harmonious synergy, cooperating for one effect." At the spinal level, as seen in reciprocal innervation, this coordination covers merely a limb or a pair of limbs. But the same mechanism of the common path extended to the play of the great arcs arising from the projicient organs of the head engages the conductive patterns of the total organism. "The singleness of action from moment to moment"

thus assured by the principle of the common path "is a keystone in the construction of the individual whose unity it is the specific office of the nervous system to perfect." As he stated succinctly, "Correlation of the activities of arcs from receptive points widely apart is the crowning contribution of the brain toward the nervous integration of the individual." [20]

MECHANISMS OF CONTROL

Prior to 1900, as we saw in Chapter IV, Sherrington had focused on facilitation, inhibition, and the sense organs and nerves of the "musculo-articular apparatus" as three basic mechanisms underlying the "elemental co-ordinations" effected by reciprocal innervation. In four papers of 1905–1906 he further examined these mechanisms in the more complex patterns of hind limb reflexes, using the new insights gained from his concept of the correlation of reflexes and the principle of the common path.

Spinal induction. From the time of his first observations of the knee jerk Sherrington had catalogued numerous cases of a temporarily depressed spinal reflex entering into a state of "exaltation," manifested by a more active, intense motor discharge. In his seventh and ninth "Notes" he analyzed three instances of this intraspinal rebound effect in hind limb reflexes: (1) in the scratch reflex after its inhibition by the crossed extension reflex, (2) in the extensor reflex after its inhibition by the flexion reflex, and (3) in the hip flexion of the mark-time stepping reflex after its inhibition by a strong squeeze of the tail.[21]

In all these cases, Sherrington reported in the ninth "Note," one sees a rebound effect of augmentation or "super-excitability" supervening on a state of spinal inhibition. He recognized the rebound effect as a form of *Bahnung* or facilitation, and felt that it was "fundamentally akin" to the phenomena of visual contrast that Hering had termed "induction." On these bases he designated the phenomenon of reflex-rebound as *successive spinal induction.*[22]

Sherrington used the word "successive" to differentiate the

rebound type of spinal induction from a form which is produced by a summation of subliminal stimuli which mutually reinforces reflex arcs from two receptive points without previous inhibition. He had described this latter species of induction in his papers on the scratch reflex, and used it as one piece of evidence for the correlation of allied arcs about a common path, prior to naming it *immediate spinal induction* in 1906.[23]

Much of the reflex action of the spinal animal's limb bears the character of an adaptation to locomotion. As the work of Sherrington and others already had indicated, several processes are undoubtedly involved in welding simpler reflexes together into the composite pattern of locomotion. Jacques Loeb had looked at the sequences which he termed *Ketten-reflexe* ("chain" or "segmental" reflexes) and indicated how a reflex in one segment may act to transfer the external stimulus to another segment and excite its reflex action, and so on. A second type of connecting process was that discovered by J. von Uexküll, who showed that a piece of musculature under static conditions that increase its length becomes more prone to excitation through its reflex arcs.[24]

In spinal induction Sherrington realized that he had found a third process "obviously qualified to play a part in linking reflexes together in a co-ordinate sequence of successive combinations." [25] Induction, he saw, is a form of facilitation especially fitted to combine the successive opposite phases of cyclic reflexes. As such, it was a phenomenon whose definition did much to explain the alternating discharge of antagonistic muscles which Sherrington had shown to be so characteristic of the mammalian spinal cord's locomotor activity.

Inhibition. By 1893 Sherrington's study of antagonistic muscle action had convinced him that inhibition is part of the normal reflex process, actively going on side-by-side with excitation. In his eighth "Note" (1905) he returned to this thesis, examining "in some particulars the conditions attaching to the initiation, and the course run by [inhibition and excitation] under comparable circumstances." [26] To define the conditions he made a detailed study of the activities of all muscles involved in moving

the knee joint, carefully analyzing the reciprocal activity of each of the antagonists.

One phase of the study concerned the ipsilateral or direct *flexion reflex,* whose salient feature is flexion at knee. In one brilliantly designed experiment a dog's hind limbs were prepared so that the knee flexors alone could act in one limb, the knee extensors alone in the other. By then applying equal stimuli to symmetrical skin points or afferent nerves in each limb Sherrington was able to delineate the characteristic features of the inhibitory and excitatory processes in the flexion reflex. The correspondences found between the processes of flexion in one limb and extension in the other "support the view that the reflex inhibition and the reflex excitation . . . although opposite in direction . . . are co-ordinated reciprocal features in one united response." [27]

In the hind limb reflexes, as elsewhere, Sherrington acknowledged once again in the eighth "Note," "the intimate nature of the process which reveals itself as inhibition is admittedly obscure," although many theories have been advanced. With these words of qualification, he presented his own hypothesis about inhibitory and excitatory processes in spinal reflexes.[28]

He established the bases for his hypothesis by reiterating four observations which he had made repeatedly:

(1) Inhibition is an active process.

(2) Its seat lies at the central end of the afferent neurone. In spinal reflexes, at least, inhibition is not equivalent to merely halting the play of an excited afferent path on a motor center. For, as seen in its immediate arrest of after-discharge, inhibition acts more rapidly than could be explained by a mere discontinuance of the afferent impulse.[29]

(3) Its central seat most probably lies in an internuncial mechanism — synapse or neurone — between the afferent and efferent neurone proper.

(4) The reflex reaction initiated from a given skin spot or nerve-twig is, with "striking invariability," either inhibitory or excitatory.[30]

On the basis of the preceding four points, each backed by

extensive experimentation, Sherrington formulated an "inference" about inhibition and excitation in spinal reflexes. In the spinal cord, he said, individual afferent fibers from the receptive field of a reflex each divide into end-branches (collaterals). When the nerve fiber is active, one set of these collaterals normally always produces *excitation* in the efferent neurone of muscle *A,* while another set always produces *inhibition* in the efferent neurones of *A*'s antagonist, muscle *B*. In brief, "the single afferent nerve-fibre would therefore be in regard to one set of its central terminal branches *specifically excitor,* and in regard to another set of its central endings *specifically inhibitory*. It will in this respect be duplex centrally." [31]

The proprioceptive system. From the time he had demonstrated conclusively that muscles possess sensory organs and nerves Sherrington had shown their importance for the production and maintenance of a host of reflex phenomena. In the 1906 issue of *Brain,* dedicated to John Hughlings Jackson, he generalized these findings in his concept of the *proprioceptive system.*[32]

At the base of his concept were certain inferences about the scope of reflexes and their relations to one another and to the broader functions of the central nervous system — inferences drawn from the distribution of *nerve receptors*. The receptors of the body, he pointed out, fall into two great groups, the *surface field* and the *deep field.* The surface field in turn may be subdivided into the *exteroceptive* or cutaneous field, richest in number and variety of receptive organs, and the *interoceptive field.* While less was known of the intero- than of the exteroceptors in 1906, Sherrington could state "with some certainty" that their field of distribution is alimentary and digestive in function and that they appear especially adapted for chemical stimuli.

The deep field presents many points of contrast to the surface field. Most notably, Sherrington felt, the stimuli effective for the two fields are fundamentally different. The deep receptors, he stated, appear adapted for "excitation by changes going

forward in the organism itself" — changes working largely through the agency of mass, with its mechanical consequences of weight and inertia, and through the mechanical strains and alterations of pressure from muscular contraction and relaxation. On the bases of their mode of excitation, Sherrington proposed that "the deep receptors may be termed *proprio-ceptors,* and the deep field a field of proprioception." [33]

Having defined "proprioception," Sherrington next considered some of its characteristics and functions. Proprioceptions, he reported, are due *secondarily* to the stimulation of the organism by the environment. Through this secondary reaction, which is habitual, reflexes arising from proprioception become attached or "appended" to and reinforce primary reflexes excited from the surface field. Secondly, he stated, proprioceptors serve to evoke compensatory reflexes, in opposite direction to those provoked from the surface.[34]

Sherrington defined the third and perhaps most important characteristic of the proprioceptors as "their tendency to induce and maintain *tonic* reactions in the skeletal musculature." Physiologists have long and often asked, he remarked, what the "utility" of skeletal muscle tonus might be. It may serve, he suggested, to assist the functioning of the muscular sense by acting on joint surfaces, tendons, and muscles. But, he added immediately, the fact that reflex tonus persists after destruction of the higher centers, "to which we have to relegate the operations of sense, and *inter alia* those of the so-called 'muscular sense'," suggests another function for tonus.[35]

Fundamentally, Sherrington held, "reflex tonus is the expression of a *neural discharge concerned with the maintenance of attitude*" — the maintenance, that is, of posture rather than movement.[36] His view of the role of tonus in the animal economy had been conditioned by observing an animal such as the decerebrate frog. The frog rests squatting in its tank in a posture very different from that which gravitation would effect were its musculature inactive, and this fact indicated to Sherrington that innervation and coordination are as necessary for the maintenance of posture as for the execution of movement.

The fact that an animal can maintain a posture with only the hind portion of its cord intact told him, too, that total posture is built from segmental posture in the normal animal. The production and maintenance of posture as well as locomotion, Sherrington perceived, involves an integration or unification of reflex actions: "reflex arcs of analogous function belonging to successive segments unite to a homogeneous reflex system extending more or less continuously through the length of the animal. Thus it is that the *proprio-ceptors and their reflex arcs have in their sum total, to be treated as a proprioceptive SYSTEM.*" [37]

Invoking the idea of "levels of control" between the head and body poles which he had expressed in his Marshall Hall Lecture, Sherrington held that the *labyrinth receptors* of the head pole are the most important and predominant part of the proprioceptive system. Because these receptors project to the hind brain, he described the cerebellum as the *head ganglion* of the proprioceptive system. The labyrinth's two major components (otolith organ and semicircular canals), he reminded his readers, are "largely responsible for the reflex posture and compensatory reflexes of the head . . . [and the labyrinth] embraces within its field of reflex effect all the segments of the body . . . [maintaining] a posture of the whole animal in regard to gravitation."

Sherrington's discussion of the labyrinth's role in the maintenance of posture was not the first, for others had previously recognized that "higher centers" such as the cerebrum, cerebellum, and labyrinth influence tonus. The elements that were new and enormously significant in his concept of the "proprioceptive system" were, first, his demonstration that the tonus of the limb muscles has an *autogenous* origin. Second, utilizing knowledge of the labyrinth's role in tonus, Sherrington pointed out that the proprioceptive system, like the common paths of spinal reflex actions, obeys a fundamental principle of integrative action in the nervous system of the intact animal: "A segmental series of reflex arcs of analogous function in its integration to a unified system tends to exhibit a functional hierarchy, in which the reflex arcs belonging to the head are supreme." [38]

THE SCRATCH REFLEX PARADIGM

Had Sherrington never delivered and published the Silliman Lectures, the corpus of his research papers along with his general addresses such as "The spinal animal," "The principle of the common path," and "The proprioceptive system," still should have marked him as biology's foremost analyst and interpreter of reflex motor behavior. These abilities are nowhere more evident than in his definitive paper on the scratch reflex (1906), in which the properties of reflexes as found in the isolated spinal cord were described minutely and fully as never before in the annals of neurophysiology.[39]

In performing his final major analysis of the scratch reflex Sherrington's techniques, as usual, were simple. The chief device was his newly developed "electric flea": a fine entomological pin, whose "bites" could be varied in frequency and strength, was inserted lightly into the horny layer of the skin where it produced no mechanical stimulus. A fine copper wire attached to the "flea's" free end formed one electrode of a faradizing circuit, the other electrode being a larger metal plate bound to the dog's bare, moistened skin. As the foot scratched in response to the electric flea's bites, its movements were traced on the smoked paper of a myograph; the records so produced illuminate the pages of Sherrington's paper. A glance at the paper's table of contents suggests the wealth of data which he thus recorded and interpreted: rhythm of reflex response, refractory phase, intensity, after-discharge, summation, immediate spinal induction, the receptive field, fatigue, spinal shock, apaesthesia, and the scratch reflex as an adapted reaction. Some of the data already had been reported in earlier papers before Sherrington brought them together, supplemented them, and gave them physiological meaning in 1906. Rather than repeat these observations or attempt to condense the paper itself, we may note just a few highlights of his analysis.

In broad terms, Sherrington stated, the scratch reflex really is a *type-reflex* composed of individual reflexes of more or less close similarity, for the reflex is not exactly the same when elicited from different parts of its receptive field. He was un-

certain how the reflex functioned as an adapted reaction in the intact animal, for he had noted that scratching never seemed actually to "comb" the parasites out. The reflex might act, he suggested, by causing a rapid and brief local extinction of the skin surface at the point irritated.

Sherrington's intensive study of reflex scratching enabled him to isolate and describe almost every physiological characteristic of reflex muscle management. He saw, for example, that the steady frequency of the reflex (about 4.8 beats per second) means that so many of the bites in a continuous series fall in a period when the reflex is *refractory* to stimuli. Further, the reflex has its own characteristically frequent *after-discharge.* "No feature of reflex reaction," he interjected, "distinguishes it from nerve-trunk or nerve-tract conduction more fundamentally than lengthy after-discharge." [40] The fact that single stimuli fail to elicit scratching told him of the importance of *summation of stimuli* in reflex response. The nature of *immediate spinal induction* in reflex scratching suggested to him that *facilitation* itself is a special form of summation.

The *paths* of the scratch reflex, he affirmed, are truly *intraspinal:* they begin and end in the cord, with no essential anatomical processes going up to higher centers. Combining his anatomical and physiological data, he attempted to assign various characteristics of reflex scratching to specific places in its reflex chain: the seat of local *fatigue* "probably" is in the first synapse of the disynaptic arc; the *refractory phase* is referable either to the descending propiospinal neurone internuncial between the receptive path and the final common path, or to the *synapse* between the propriospinal neurone and the motor neurone of the final common path; *immediate spinal induction* is referable to the internuncial propriospinal neurone.

Sherrington's analysis of the scratch reflex and other hind limb reflexes, such as flexion and extension, inaugurated a new and fuller era of neurophysiological research. By following a simple but rigorous course of methodical tests he had, in the words of E. G. T. Liddell, "minutely cross-examined the spinal

cord on its evidence," unveiling and charting the characteristics of its reflex pathways.[41]

The scratch reflex was the last such large piece of reflex "machinery" that Sherrington analyzed. The data it yielded, showing how many nerve units are coordinated for a single, complex, purposeful neuromuscular act, made him see more clearly than ever the complex nature of reflexes and the intricacy of the central physiological mechanisms behind them.

A new conception of the nature of reflexes and their role in the animal economy clearly was demanded by Sherrington's data, and was duly supplied in the concept of integrative action. After 1906 and the publication of *The Integrative Action,* problems which the scratch and other hind limb reflexes had raised afresh — such as how excitation is built up in spinal centers until the final motoneurones are discharged — continued to provide a paradigm that guided him to the isolation and functional analysis of the motor unit in 1930.

VII

Reflexes and Motor Integration

The nervous synthesis of an individual from what without it were a mere aggregation of commensal organs resolves itself into co-ordination by reflex action.
— *The Integrative Action of the Nervous System*

THE SILLIMAN LECTURES

In 1904 the forty-seven-year-old Charles Sherrington journeyed with his wife from Liverpool to New Haven, Connecticut, to become Yale University's second Silliman Memorial Lecturer.[1] Before departing for Yale, Sherrington wrote with characteristic modesty to Harvey Cushing: "[I] possess misgivings of a serious character as to my shortcomings for the Silliman Lectureship. Mais il faut de l'audace, et encore de l'audace, et toujours de l'audace." [2]

Any of Sherrington's "misgivings," as we shall see, should have centered only on his lecture style. He was a great personal success at Yale, and, in the opinion of Professor R. H. Chittenden, chairman of the Silliman Lecture Committee from 1903 through 1922, the publication of his lectures "brought more credit to the University than any of the other books of the series." [3]

The Sherringtons' stay in New Haven was a busy one, with rounds of entertainment by members of the Yale faculty, visits to the Yale Laboratories, where Sherrington "frequently gave valuable suggestions to the workers he found there," and lengthy walks about the New Haven area.[4] Perhaps the most delightful expression of Sherrington's popularity at Yale came on May 3, when he was given a dinner at the Yale dining hall. The affair was organized chiefly by Yandell Henderson, and approximately sixty guests gathered to pay informal tribute to the Silliman Lecturer — a tribute uniquely stated in the "Sherringtonian" terminology of the dinner menu (Fig. 7).

Sherrington delivered ten lectures on "Integrative action by the nervous system" at Yale's North Sheffield Hall between Fri-

day, April 22, and Wednesday, May 4. The sessions, recalled Professor Chittenden, "were very well attended; though naturally technical they drew a large audience, many ladies being present owing I presume to the great popularity of Mrs. Sherrington." [5] Anyone who had known Sherrington might have predicted the mixed reactions of his audiences at the lectures. For, as Lord Cohen succinctly remarked, throughout his long career Sherrington "was not classed among the more successful lecturers . . . He eschewed dogmatism, he fought for the . . . word or phrase to convey precisely his meaning so that he appeared unduly hesitant; he qualified his statements, he inserted parentheses; indeed he gave the impression that his thoughts were not really in the lecture room but already contemplating and designing another experiment." [6]

SYLLABUS	PROTOCOLS
***	***
Gastronomic Experiments for the development of AN INTERNATIONAL SYNAPTIC SYSTEM	Some of Nature's First Experiments With the Synaptic System on the half shell
integrating	Applications of Carmine Staining Fluid with a spoon
Certain Newly Medullated Neurons	Ultramarine Brain Food Starvation Army Staple
with	Metameres of Skeletal Musculature From A Higher Vertebrate
THE HIGHER CENTER	Decerebrated Squab Exhibiting Toastotropism
Professor C. S. Sherrington, M.D., LL.D., F.R.S. Silliman Lecturer	Verdant Proprionociceptor Alleviator
Accompanied by Explosions from Broca's Convolution by the Biological Quartet	Proteid Secretion of Hypertrophied Sebaceous Glands
Concluded by	Microtome Sections by Freezing Process
Demonstrations by Professor Mendel on Various Human Subjects: Scratch Reflex, Knee Jerk, Shivering, Spinal Shock	Saccharine Stimulus of Trigeminus
Summary of Results Professor Sherrington	Caffeine For Vaso-Motor Reactions

Fig. 7. *The Sherrington Dinner Menu* (*Fulton papers*).

According to the review of the Silliman Lectures written by Yandell Henderson for the *Yale Alumni Weekly,* Sherrington's "attitude toward his task . . . was not to instruct but to suggest." Throughout the lectures, Henderson felt, Sherrington "showed himself rather the investigator than the lecturer." By formulating a question the researcher has often gone more than halfway toward answering it, and in this vein Sherrington "frequently neglected questions now formed and awaiting answer, for those matters out of which the questions of the future will arise." [7]

The effect of such a mode of presentation upon the audience, Henderson continued, was "strikingly paradoxical."

> To him who had devoted thought and study to the nervous mechanisms of the animal body, the discussions were either very suggestive or so abstract to be difficult to follow. To the laymen present . . . the same matters seemed so simple and self-evident as to be mere truisms. This is well illustrated by the comments of one of these gentlemen who, though neither a physicist nor a physiologist, attended some of the lectures of Professor Thomson last year and as many of Professor Sherrington. Of the former he remarked: 'I understood all the words; but I sat there for an hour, and I did not know a thing the man had said; and I thought that was fine.' Of Professor Sherrington's lecture on the 'Scratch Reflex' he remarked: 'I understood the whole of it. Everyone knows how a dog scratches himself when a flea bites him.' Evidently in this case such unfamiliar phenomena as those of the radium emanation seemed more impressive and better entitled to discussion in the University's most highly endowed lectures, than the often observed, and therefore commonplace, movements of an animal's legs.

The Integrative Action of the Nervous System

Despite the mixed reactions which Sherrington's delivery of the Silliman Lectures evoked, their publication in 1906 was recognized as an epochal event for the development of neurophysiology. Writing in the *British Medical Journal,* F. W. Mott observed that both Sherrington and J. J. Thomson, the first Silliman Lecturer, "have contributed in their respective domains of science . . . to the advancement of natural knowledge in a degree unsurpassed by any of their contemporaries." [8]

Dedicating his book to David Ferrier, whose researches had helped to interest him in neurophysiology, Sherrington entitled it *The Integrative Action of the Nervous System.* His choice of a title came after great deliberation, for, as E. G. T. Liddell commented, Sherrington "used to spend a lot of time in choosing words." Thus, he considered and abandoned the Lectures' original title, "Integrative action by the nervous system," and a second alternative, "Integration in the nervous system," before selecting the words which are now practically synonymous with his name.[9]

In the sixty years since its publication, *The Integrative Action* has been reprinted five times: in 1911, 1914, 1916, 1947, and 1961. A revised second edition was suggested by the Yale University Press to John Fulton in 1932, when the book was out of print, but Fulton reacted strongly against the idea of textual revision. He wrote to Sherrington on March 3, 1932:

> I ventured to explain [to the head of the press] that revision of the book after so long a period would be exceedingly difficult but that I thought you might possibly be willing to prepare a preface which would give some idea of the relation of recent work to the conception of integration. To touch the original text would be like attempting to rewrite [Harvey's] *De Motu Cordis*!
>
> The demand for the book continues to be very considerable and it would be a great pity if the book should become no longer available to students.[10]

When *The Integrative Action* again was issued, in 1947, it differed from the original only in its reset type and illustrations and in the addition of a foreword by Sir Charles dealing with his more recent views on the concept of integrative action. The 1947 reprinting, published in England by the Cambridge University Press, was sponsored by the Physiological Society under the editorship of Samson Wright. The book was prepared as a special gift for the members of the Seventeenth International Congress of Physiology, who gathered at Oxford in July 1947 for their first meeting since that held at Zurich in 1933.

The lasting value of *The Integrative Action* for students of the nervous system is reflected clearly in the numerous reviews of the 1947 reprint. F. M. R. Walshe, writing in the *British Medical Journal,* said:

I have called it 'an imperishable work,' for it is one of those works, rare in science, the permanent value of which is unquestionable, and I believe that future generations of physiologists will so acclaim it. In physiology, it holds a position similar to that of Newton's *Principia* in physics . . . For it is more than an orderly record of precise observations: it is a product of sustained thought upon what is essentially — though only his genius revealed it as such — a single problem — namely, the mode of nervous action. . . . the principles of reflex action that he expounded will remain essential foundations of whatever edifice of knowledge may yet be erected upon them. The book is a primer for every physiologist and student of clinical neurology — indeed, for every medical man who values the study of precise observation and its integration into ordered knowledge as part of a scientific teaching.[11]

The book which Walshe termed the *Principia* of physiology consists, in essence, of a synthesis of Sherrington's own researches and concepts and a chronicle of relevant work by other investigators. In its latest issue (1961) the book's ten Silliman Lectures total 390 pages, with 85 figures. A bibliography of 314 items, 22 of them Sherrington's publications, ranges from the writings of seventeenth-century workers such as Descartes to research papers published in 1905.[12]

The Integrative Action is not an easy book to assimilate, first of all because of the vast amount of material which it contains. Moreover, Sherrington's style, characterized by long and complex sentences, is hard to follow at first. In writing, as in lecturing, he sought to convey his meaning precisely and unequivocally — a doubly difficult goal to realize when gearing a book for both a lay and professional audience.

For our purposes — a look at the structure and the major concepts of *The Integrative Action* — the book may be divided into six parts: (1) Sherrington's definition of his topic in the first seven and one-half pages of Lecture I, (2) Lectures I–III: coordination in the simple reflex, (3) Lectures IV-VI: coordination between reflexes — their interaction and compounding by simultaneous and successive combination, (4) Lecture VII: reflexes as adapted reactions, (5) Lectures VIII–IX: the brain, and (6) Lecture X: sensual fusion.[13]

THE SCOPE OF *The Integrative Action*

Sherrington's written analysis of the integrative action of the nervous system followed basically the same pattern as his research work. He began by delineating the characteristics of the simple reflex, the smallest functional unit of integrative action as seen in the spinal animal, and then built toward the complex patterns of reflex muscle management, guided by the brain, in the intact animal.

For a person unfamiliar with Sherrington's work, the first seven and one-half pages of the Silliman Lectures provide an essential and succinct definition of the meaning and scope of the integrative action concept.[14] As in his "Common Path" address of 1904, Sherrington began by defining three main lines of neurophysiological research. Nerve cells may be studied, like all cells, as living units; in terms of their characteristic feature, conduction; and in their *integrative functions.*

Sherrington broadly defined the "integration of the [multicellular] animal organism" as the welding together of a "mere collection of organs" into an "animal individual" (p. 2).[15] Such integration, he observed, is possible in part because the structure of multicellular organisms permits the operation of *intercellular* activities in addition to intracellular and cell surface ones. By a brief comparison of modes of intercellular integration he clearly depicted the uniqueness of the nervous system's structure and functions, a system which he viewed as "in a certain sense the highest expression of the *milieu interne*" (p. 4).[16] The integrative capabilities of both solid and fluid intercellular materials, he pointed out, are limited, for they are not "after all [a] living channel of communication, delicately responsive to living changes though [they] may be" (p. 4).[17] It is the living bond of the nervous system, Sherrington emphasized, that is employed when the organism needs precise speed and fine temporal and spatial adjustments for activities such as movement. "It is in view of this interconnecting function of the nervous system that the field of study of nervous reactions which was called at the outset the third or integrative, assumes its due importance. The due activity of the interconnexion resolves

itself into the co-ordination of the parts of the animal mechanism by reflex action" (p. 5).

With these words Sherrington defined the special role of the nervous system's integrative action in the animal economy and identified its unit phenomenon, the *reflex.* He next noted that in complex organisms such as vertebrates at least three separable structures, components of a *reflex arc,* are involved in producing a reflex action: (1) a *receptor* or initiating organ, (2) a conducting nervous path (*conductor*) with at least two nerve cells, one connected with the receptor, one with (3) an *effector* organ, such as muscle. Following his analysis of the reflex arc's structure he explained why the reflex arc is the unit mechanism for integrative nervous functions. "The unit reaction . . . is the reflex, because every reflex is an integrative reaction and no nervous action short of a reflex is a complete act of integration. The nervous synthesis of an individual from what without it were a mere aggregation of commensal organs resolves itself into co-ordination by reflex action" (p. 7).

Sherrington's study of vertebrate motor behavior had shown, however, that not every reflex is a unit reaction, for some reflex actions are compounded of simpler reflexes. Therefore he distinguished between *two grades of coordination.* The first grade is that *by the simple reflex:* a given effector responds to a given receptor with all other parts of the body indifferent to and unnecessary for the reaction. Sherrington realized that a simple reflex is "probably a purely abstract conception," for the nervous system is completely interconnected and never absolutely at rest, making it unlikely that any one part can react without affecting, and being affected by, some other part. But for practical purposes, as he had discovered, the simple reflex is a "convenient, if not probable, fiction," enabling a researcher to analyze the characteristics and components of complex reflexes (p. 7).

He defined the second grade of nervous coordination as *the coordination of reflex actions.* As he had found by observing the play of skeletal musculature during motor behavior, this grade involves two phases. First, a number of simultaneously occurring simple reflexes are coadjusted into an orderly "reflex

pattern." Secondly, there must be orderly changes from one reflex pattern to another, a "co-ordination of reflexes successively proceeding" (p. 8).

In his brief introduction to *The Integrative Action* Sherrington thus laid down three central propositions: the nervous system is a, if not the, major integrating agent in complex multicellular organisms; the reflex is the unit reaction in nervous integration; there are two grades of reflex coordination: that effected by the simple reflex, and that by the simultaneous and successive compounding of reflexes. Working from these premises he proceeded to demonstrate in meticulous detail how "the main secret of nervous co-ordination lies . . . in the compounding of reflexes" (p. 8).

COORDINATION IN THE SIMPLE REFLEX

Sherrington viewed the analysis of the simple reflex much as he had his mapping of sensory and motor pathways — as a necessary "preliminary step" for understanding reflex interactions. He reflected this orientation when he stated that the first three Silliman Lectures, nearly one-third of the text, are devoted to "clearing the way toward the more complex problems of co-ordination" by considering the nature of coordination in the simple reflex (p. 8). He set the dominant theme of his analysis of the simple reflex with the statement that "from the point of view of its office as integrator of the animal mechanism, the whole function of the nervous system can be summed up in one word, *conduction*" (p. 8).

The receptor. Before turning to the topic of conduction, Sherrington asked what characteristics of the functioning of the reflex arc are probably determined by the receptor. In answering this question he introduced a theme which runs through *The Integrative Action*: the principles of biological evolution — natural selection and adaption to the environment — underlie the nature of nervous integration in vertebrates.

As its name implies, Sherrington observed, the receptor is a structure which "adaptation has specialized for excitation of a

kind different from that obtaining for all the rest of the arc" (p. 9). The reflex receptor, in brief, is concerned with the *mode of excitation,* and, as seen in the particular types of stimuli which effectively elicit different reflexes, its main function is *selective excitability.* The receptor's attribute of selective excitability, Sherrington asserted, contributes to reflex coordination in two ways. By making an arc receptive to certain kinds of stimuli, kinds to which other arcs are less responsive, it increases the organism's responsiveness to its environment. By limiting the effectiveness of particular stimuli to particular bodily regions, the receptors help to prevent "confusion of reactions (inco-ordination)" (p. 13).

Reflex arc conduction. Simple reflex coordination is expressed when an effector makes a response appropriate to the stimulus impinging on the arc's receptor. This "due propriety of end effect," Sherrington maintained, "is largely traceable to the action of the conductor mediating between receptor and affector [*sic*]" (p. 9). In large measure, obviously, conduction in reflexes is conduction along nerve trunks. Yet, as Sherrington's years of studying the characteristics of spinal reflexes had shown, "reflex conduction *in toto* differs widely from nerve-trunk conduction" (p. 13). Utilizing data gathered since the time of Robert Whytt, Sherrington made one of his major contributions to neurophysiology by cataloguing and analyzing the major characteristics distinguishing reflex arc from nerve trunk conduction:

(1) slower speed as measured by the latent period between application of a stimulus and appearance of end-effect, this difference being greater for weak stimuli than for strong; (2) less close correspondence between the moment of cessation of stimulus and the moment of cessation of end-effect, i.e., there is a marked 'after-discharge'; (3) less close correspondence between rhythm of stimulus and rhythm of end-effect; (4) less close correspondence between the grading of intensity of the stimulus and grading of intensity of the end-effect; (5) considerable resistance to passage of single nerve impulse, but a resistance easily forced by a succession of impulses (temporal summation); (6) irreversibility of direction instead of reversibility as in nerve-trunks; (7) fatigability in contrast with the

comparative unfatigability of nerve-trunks; (8) much greater variability of the threshold value of stimulus than in nerve-trunks; (9) [a] refractory period, [b] 'bahnung', [c] inhibition, and [d] shock, in degrees unknown for nerve-trunks; (10) much greater dependence on blood-circulation, oxygen; (11) much greater susceptibility to various drugs-anaesthetics (p. 13).

Sherrington's exploration of these characteristics fell into two broad parts. First, he typically sought to establish an anatomical and physiological substrate for the uniqueness of conduction along reflex pathways. Secondly, he analyzed the characteristics themselves, giving an experimentally supported description of each phenomenon and its known or probable function in reflex coordination.[18]

The synapse. As he had been doing since the 1890's, Sherrington explained why the differences between reflex arc and nerve trunk conduction are referable to that part of the arc which lies within the gray matter: specifically, to the surfaces of separation or synapses between adjacent neurones in the gray matter.[19] "We know of no reflex-arc," he wrote in *The Integrative Action,* "composed of one single neurone only . . . The reflex-arc must, therefore, on the cell theory, be expected to include not only *intracellular* conduction, but *intercellular* conduction. But on the current view of the structure of the nerve-fibres of nerve-trunks the conduction observed in nerve-trunks is entirely and only *intracellular* conduction. Perhaps, therefore, the difference between reflex-arc conduction and nerve-trunk conduction is related to an additional element in the former, namely, *inter*cellular conduction" (p. 15).[20]

The characteristics of reflex arcs. Proceeding from his conviction that the characteristics of reflex arc conduction are referable largely to *events at the synapse,* whatever the exact nature of those events might be, Sherrington turned to the characteristics themselves. As he had found in his researches, "notable differences" between reflex arc and nerve trunk conduction are revealed by the *"internal condition"* of the central nervous system, such as its oxygen and blood supply and the presence of poisons and drugs (items 10 and 11) (p. 80).

Most of the differences, however, can be delineated by a precisely designed and executed "input-output" analysis, chiefly an exploration of the stimulus-response relations of reflex pathways under given variables. It is primarily with the phenomena revealed by the latter course of study that Sherrington deals in Lectures I–III. His discussion rests chiefly upon studies of reciprocal innervations and the hind limb reflexes of the spinal dog, and is accompanied by thirty-six illustrations, mostly myograph tracings from his experiments (Fig. 8).

Stimulus-response rhythm, stimulus-response intensity, stimulus summation, threshold of excitability, and direction of conduction (items 3, 4, 5, 8, and 6) were five of the more clearly defined aspects of reflex action at the turn of the century. Sherrington's treatment of them was brief, amounting to little more than an experimentally couched description of each phenomenon and a short statement of its known or presumed role in producing a coordinated simple reflex. He had, in turn, found latency, after-discharge, the refractory phase, and inhibition (items 1, 2, 9a, and 9c) to be four of the most prominent, most complex, and perhaps most significant characteristics of reflex arc conduction. Accordingly, he devoted the bulk of his discussion of coordination in the simple reflex to analyzing these four phenomena.

Latency, the time lapse between stimulus application and the appearance of a reflex response, and *after-discharge,* the period between stimulus cessation and response cessation, are examined in the last half of Lecture I.[21] Considering the effects of latency and after-discharge upon the production and maintenance of a reflex response, Sherrington figuratively described them as indicating "inertia" and "momentum." Using a simple and fruitful analogy from mechanics, he suggested that "it is as though in the case of a weight to be pulled from a position of rest the tractive force were applied through a rigid rod in nerve-trunk conduction, but through a relatively yielding elastic band in reflex-arc conduction" (p. 35).

Sherrington's exploration of the next two key characteristics of reflex arc conduction, the *refractory phase* and *inhibition,* occupied nearly half of the second and third Lectures, respec-

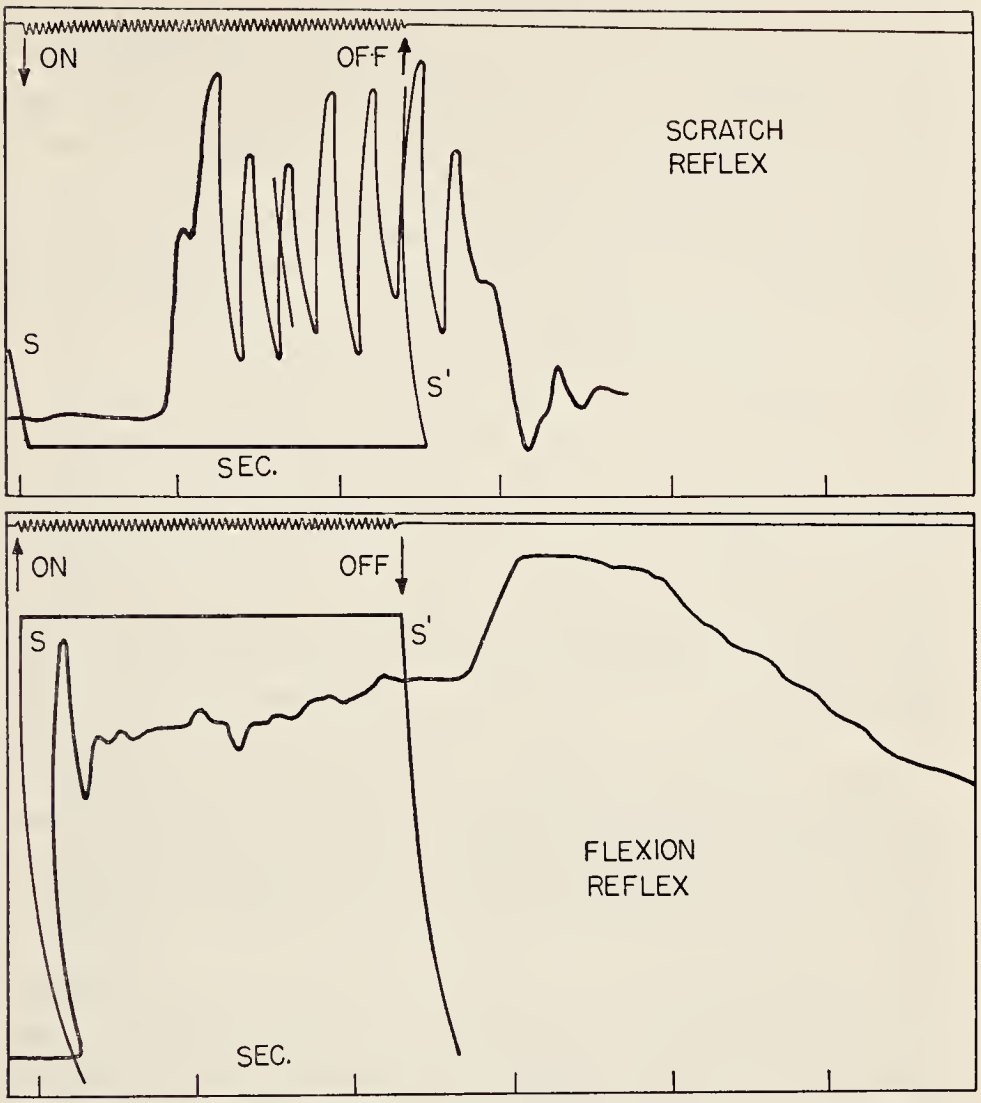

Fig. 8. *After-discharge.* Comparison of scratch-reflex and flexion-reflex provoked by similar stimulation in the same animal in quick succession. Records from above downwards for scratch-reflex (above) and flexion-reflex (below):

Period of stimulation. An electromagnet in the primary circuit records the interruptions giving the shocks.

Myograph curve: the vertical arcs show the onset (*S*) and cessation (*S'*) of stimulation (also shown by the arrows ON and OFF).

Time in sec.

Stimulation was unipolar faradization with 45 break shocks; the kathode was stigmatic and applied to the shoulder skin for scratch-reflex, to the fourth toe for flexion-reflex; diffuse electrode on the fore-foot. Frequency of shocks, 18 per sec. The after-discharge of the scratch-reflex lasted barely 1 sec.; that of the flexion, nearly 8 sec.

tively.[22] A central theme in his analysis of the refractory phase was a comparison of the phenomenon in the swimming-beat reflex of Medusa and the scratch reflex of the dog, a comparison which yielded many insights into the increasing complexities of nervous integration in the evolutionary scale.[23]

There are several functional resemblances between the refractory phase in Medusa's swimming and the dog's scratching, for, as Sherrington said, the "refractory phase appears . . . at one end and at the other of the animal scale as a factor of fundamental importance in the co-ordination of certain motile actions." He felt, however, that the one significant difference between the refractory phases in the two organisms was more instructive than their similarities. In Medusa the refractory state is intimately connected with the *peripheral* organ, probably as a function of its unpolarized nerve-net, while in the scratch reflex it has an intraspinal, *central* seat, "remote from the peripheral tissue in whose function it finds expression" (pp. 42, 43).

Medusa's "mechanical organ," its swimming bell, can perform only one movement. Swimming, Sherrington stated, is the "one purpose demanded from it by each of all the receptor channels playing upon it" (p. 64). But the scratch reflex's "mechanical organ," the hind limb, is a complex structure: it can reflexly stand, squat, walk, run, and gallop in addition to executing a clonic scratching movement. Thus, Sherrington realized, it must be possible for reflex scratching to be replaced by other limb reflexes, many of which would be "defeated" by clonic action. Here, he saw, is the value of a central site for the refractory phase, for a central locus permits the supervention of other kinds of reflexes while the scratch reflex is refractory to its effective stimuli.[24] In sum, Sherrington held that in evolutionary terms the transition from a peripheral to a central refractory phase becomes a key mechanism for the compounding and successions of reflexes that ensure animal integration.

Sherrington recognized that the refractory phase is "obviously akin" to a state of *inhibition,* for it prevents "that confusion which would result were refractory phase in some of the arcs allowed to concur with excitatory phase in others" (pp. 65, 63).

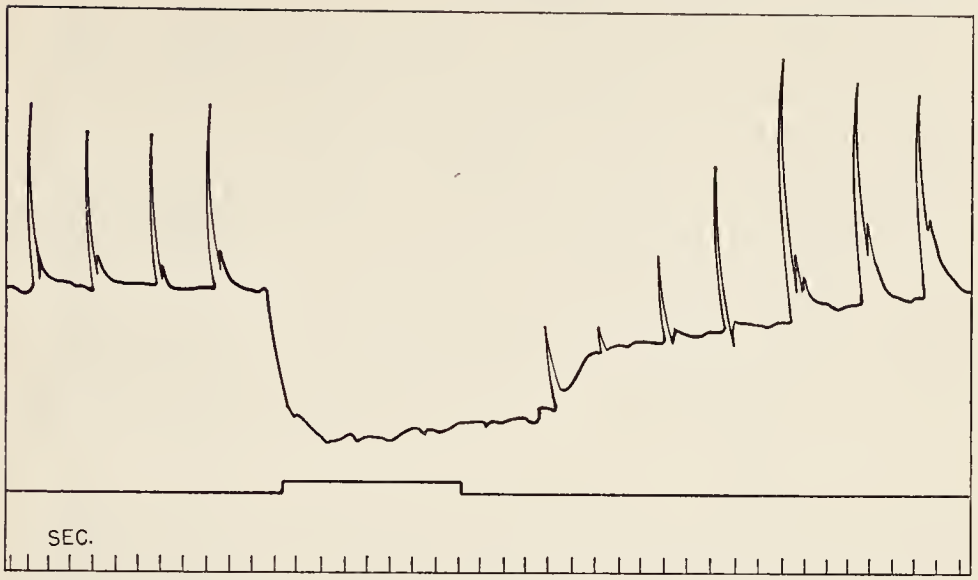

Fig. 9. *Reflex Inhibition of the Knee Jerk.* Records from above downwards:
Tracing from preparation of the extensor muscles of the knee, recording a series of knee-jerks elicited at each alternate beat of a metronome.
Signal line: Weak faradization of the central end of the hamstring nerve was applied during the time marked by the rise of the signal.
Time in sec.
At the onset of stimulation the tonus of the extensor muscles at once fell and with it the knee-jerk was temporarily abolished. After cessation of the inhibiting stimulus the tonus and the knee-jerk quickly returned, and the latter became more brisk than previous to the inhibition.

Inhibition, as we would expect from Sherrington's work on reciprocal innervation, is an important subject in *The Integrative Action.* He introduced *reciprocal inhibition* (Figs. 9 and 10) in Lecture III, basing his discussion chiefly upon the first eight "Notes" in the *Proceedings of the Royal Society.*

He began his analysis of inhibition by defining two new terms: *reflexes of successive double-sign,* and *reflexes of simultaneous double-sign.* In the end effect of certain reflexes, such as the scratch and eyelid reflexes, a phase of excitation is suppressed by a state of inhibition. If stimulation is continued, Sherrington found, one sees a continuous succession of these two phases, excitatory and inhibitory. "If we denote excitation as an end-effect by the sign *plus* (+), and inhibition as end-effect by the sign *minus* (—), such a reflex as the scratch reflex can be termed a reflex of [successive] double-sign" (p. 83). Flexion and

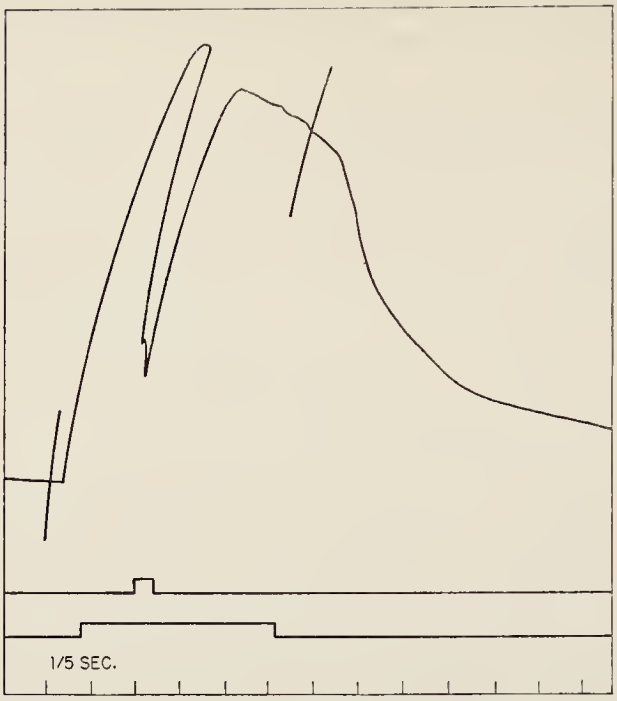

Fig. 10. *Inhibition of Crossed Extensor-Reflex.* Records and procedures: lower signal and vertical arcs indicate contralateral stimulation producing crossed extensor-reflex. The inhibiting stimulus (upper signal) in this instance was weak faradization applied to the proximal end of the severed "hamstring nerve."

crossed extension reflexes, in turn, illustrate "simultaneous double-sign: . . . the end-effect consists both in excitatory state and in inhibitory state, but the inhibitory state does not supervene on the excitatory or have the same locus of incidence as the excitatory; it occurs simultaneously with it at another interrelated locus . . . The end-effect of the reflex is expressed by two groups of muscles whose contractions act in opposed direction at the same joints" (p. 83).

Here, under a new name, is the process which Sherrington had shown to be so basic for elemental coordination — the *reciprocal innervation* of antagonistic muscles.

Having introduced the phenomena of double-sign reflexes Sherrington devoted sixteen pages to discussing the forms in which central inhibition in general, and reciprocal innervation in particular, may occur.[25] He then concluded Lecture III by presenting two important hypotheses. First, he proposed an idea

originally presented in the discussion of reflex arc competition in his "Common Path" address: "The preclusion of the motor neurone from one reflex while it is still left open to it to respond to other reflexes appears to be one of the services of inhibition to the organism" (p. 103). Second, drawing from his eighth "Note," he stated his concept of the neuroanatomy of reflex inhibition and excitation: "the nerve-fibres from the receptive field of the reflex each divide in the spinal cord into end-branches (e.g. collaterals), one set of which, when the nerve-fibre is active, produces excitation, while another set . . . produces inhibition" (p. 104).

By the time he has read the hypothesis above, a reader of *The Integrative Action* has learned virtually all that was known or hypothesized in 1906 about the operation of the reflex arc, the unit mechanism of integrative nervous action. Following the pattern of his own researches, Sherrington analyzed the operation of reflex arcs in single muscle and nerve pathways, in "simple reflexes" such as the knee jerk, and in more complex pathways such as the scratch reflex of the spinal dog. By following this analysis the reader learns the nature of the reflex responses that can be made to occur with an almost mechanical precision in the spinal animal. Simultaneously, he sees how Sherrington's careful step-by-step comparison of these reflex responses with the known characteristics of conduction in nerve trunks revealed the physiological characteristics and bases of coordination in the "simple reflex."

In sum, Sherrington showed first that the striking differences between reflex arc and nerve trunk conduction depend on the presence of synapses in the gray matter of the spinal cord through which reflex pathways course. Secondly, he demonstrated that it is the presence and interaction of the characteristic phenomena of reflex arc conduction, combined with the selective excitability of the receptor, which makes possible the coordinated nature of a simple reflex response. The reflex centers of the spinal cord, as he had first pointed out in his anatomical work, are assemblages of many anatomical and physiological components, but they operate as functional units. "Each

of the various types of simple reflex possesses to a large extent its own peculiarities of conduction. Though there are differences between conduction in various nerve-trunks . . . these differences sink to insignificance when contrasted with the extent and variety of the conductive differences exhibited by different reflex-arcs. And in the case of each reflex-arc its idiosyncrasies of conduction form an obvious basis for the co-ordination exhibited by its reflex-act" (p. 81).

REFLEX INTERACTIONS

Sherrington's discussion of "double-sign reflexes" in Lecture III at once concluded his analysis of coordination in the simple reflex and paved the way for the subject matter of Lectures IV–VI: the formation of complex reflex patterns by the processes of simultaneous and successive combination.[26] He began Lecture IV by showing how this "second grade" of reflex coordination is made possible by a major architectural feature of the synaptic nervous system — the structuring of reflex arcs into *private, common,* and *final common paths* (see Fig. 11).

Whether an animal is intact or spinal, there is a constant play of reflexes about any given common path. For, as Sherrington explained, "the usual thing in nature is not for one exciting stimulus to begin immediately after another ceases, but for an array of environmental agents acting concurrently on the animal at any moment to exhibit correlative change in regard to it, so that one or other group of them becomes — generally by increase in intensity — temporarily prepotent" (p. 120). In his 1904 "Common Path" address Sherrington had pointed out that the various types of reflexes competing for temporary use of a final common path fall into two broad classes: cooperative and competitive. A more detailed analysis of these two classes, now termed *"allied"* and *"antagonistic"* reflexes, formed the major focus of his fourth through sixth Silliman Lectures.

Reflex interaction: simultaneous combination. Antagonistic reflexes stand in an inhibitory relation to each other and thus can interact only successively. Consequently, reflex compound-

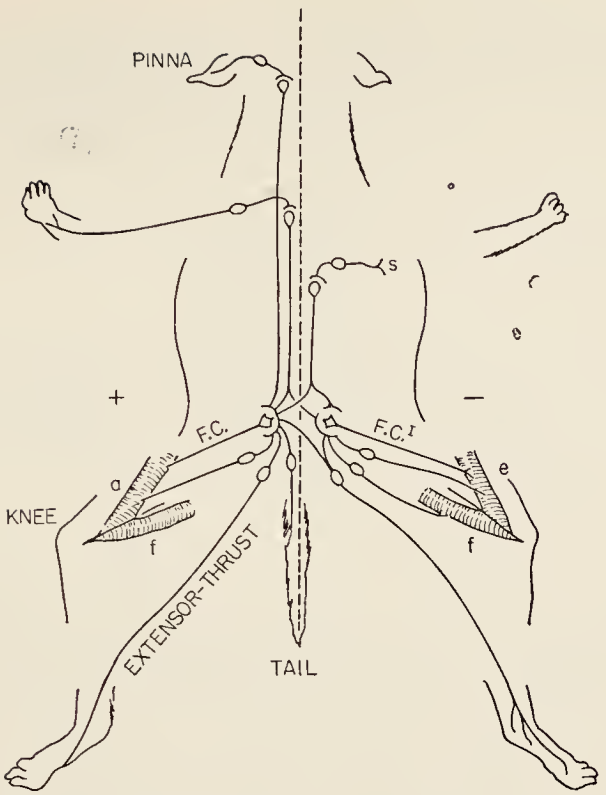

Fig. 11. *The Operation of the Common Path.* The play of reflexes upon the final common path is illustrated in this diagram of the paths of certain type-reflexes. *FC*: final common path, in this example the motor neurone of a dog's or cat's vastus crureus muscle; *s*: scratch receptor; *e* and *f*: extensor and flexor muscles of the knee. Reflexes acting as "allied reflexes" on *FC* are represented as having their terminals joined together next to the final common path. Reflexes with excitatory effect (+) are shown brought together on the left, those with inhibitory sign (—) on the right, to indicate that reflexes initiated from corresponding points in the two halves of the body are commonly antagonistic.

ing by the *simultaneous combination* of reflexes involves only the interaction of *allied reflexes.* Alliance, Sherrington explained in Lectures IV–V, is a mutual reinforcement of reflexes resulting in the simultaneous correlation of their end effects, and may occur in three forms: *allied excitatory, inhibitory,* and *double-sign reflexes* (pp. 129–137). Allied excitatory or inhibitory reflexes, he had found in turn, occur among four important classes of reflexes:

(1) Excitatory or inhibitory alliance occurs readily between

individual reflexes belonging to a type-reflex such as scratching. Type-reflexes permit simultaneous combinations to occur widely and readily, as the extent of each type-reflex's receptive field is usually wide. The coalescence of allied arcs within the receptive field of a type-reflex, Sherrington observed, "tends to make weak stimuli applied to an extensive area equivalent to intenser stimuli applied to a smaller area" (p. 130).

(2) Alliance within a type-reflex may be aided by a second form of alliance: *reflex complication.*[27] In reflex complication receptors or different species (that is, mechanical, thermal) within the same receptive field may excite allied excitatory or inhibitory reflexes.

(3) The third important class of allied relations embraces *proprioception.* Alliance may occur between proprioceptive reflexes themselves, or, as is habitually the case, between the extero- and proprioceptive components of a type-reflex such as flexion.

(4) Finally, Sherrington observed that alliance may occur between a wider combination of reflexes than the regularly studied type-reflexes: "The motor neurones of a muscle of the knee are the *terminus ad quem* of reflex-arcs arising in receptors not only of its own foot, but from the crossed fore-foot and pinna, and tail, also undoubtedly from the otic labyrinth, olfactory organs, and eyes. Thus, if we take as a standpoint any motor-nerve to a muscle it consists of a number of motor neurones which are more or less bound into a unit mechanism" (pp. 135–136).

As Sherrington had found in the researches leading to his "rules" of reflex action, a major process underlying all these forms of reflex alliance is *irradiation*: the spatial spread of a motor impulse over long or short paths from a focus of reflex discharge. In his fifth Lecture he reviewed the nature of irradiation, presenting his own "rules" and the anatomical data on which they rested, and once again attacking Pflüger's "laws." The extent and direction of irradiation, he emphasized, is a

function of several factors — stimulus intensity, the lines of conduction afforded by the given neural paths, and, most important, the neurone threshold (see Fig. 12).

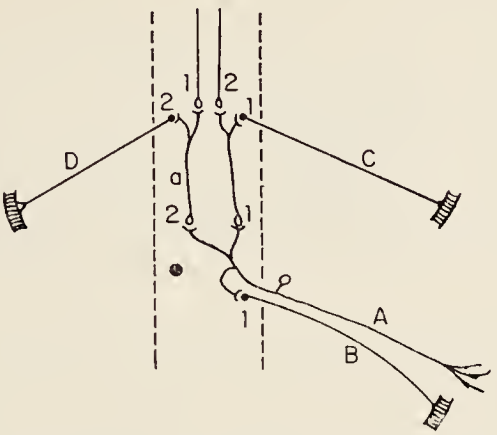

Fig. 12. *The Neurone-Threshold and Irradiation.* As schematically shown in this diagram, Sherrington held that a reflex action "irradiates" or spreads along certain conductive arcs more readily than along others because of differences in the facility of conduction at different synapses. Each synapse, he asserted, has a "neurone-threshold," a threshold value for the stimulus strength necessary to excite it.

Receptive neurone *A* enters the cord and synapses with three neurones; the neurone threshold is higher (*2*) at one of the synapses than at the other two (*1*). Each of the intraspinal neurones, in turn, synapses with two neurones, and in these cases too the thresholds are of different heights (*2* and *1* respectively).

With regard to reflex arcs *A-B*, *A-C*, *A-D*, Sherrington wrote, "it is impossible to predict exactly how the resistance will sum along the whole conductive chain . . . Yet it is clear that the threshold for any whole arc cannot be lower than the highest individual threshold in it. Further, the individual thresholds will tend to sum . . . Thus, with even small grades of difference of threshold at different synapses, large differences in the conductive facility of different reflex-arcs can be established."

In his fourth and fifth Lectures, in summary, Sherrington showed that the compounding of reflexes by the simultaneous combination of allied arcs allows the organism a wide range of coordinated movements. The facts of irradiation, he saw, indicate that there are few if any mutually indifferent reflex arcs in the central nervous system — a condition underlying that system's integrative capabilities. Thus, within a single receptive field, irradiation permits the synthesis of many separate re-

sponses into a type-reflex such as scratching. Irradiation over long paths, in turn, yokes motor mechanisms from different receptive fields and so affords channels of communication between distant receptors and effectors in the body.

Reflex interaction: successive combination. The second facet of the compounding of reflexes involves their successive combination. Sherrington's discussion of successive combination in Lecture VI falls into three parts: the sequence of allied reflexes, the sequence of antagonistic reflexes, and factors determining the sequence of reflexes competing for dominance of a common path.

(1) *Allied succession.* The succession of one reflex by another allied reflex, Sherrington pointed out first, is a common occurrence. As in the case of a flea traveling over the skin-field of the scratch reflex, any stimulus moving over a receptive field is apt to link allied arcs successively. Second, he stated that the factors shaping the simultaneous combination of allied arcs, such as stimulus incidence, immediate induction, and neurone threshold, also affect their successive combination.[28]

In his researches Sherrington had observed that if two successively allied reflexes are very similar, it is hard to determine at what moment the transition from one to another occurs. But if the reflexes are recognizably dissimilar (for example, high and low scratch reflexes) the moment of transition is obvious, for there seems to be no period of summation between the responses to their respective stimuli. In this latter case, he wrote, "there is [an] absence of any period of fusion of the two reflexes. Such fusion might appropriately be termed confusion. The rule seems that such confusion is avoided in the transition" (p. 188).[29]

(2) *Antagonistic succession* (see Fig. 13). There is an even greater need in the animal economy for antagonistic reflexes to succeed one another without a "period of confusion." For, Sherrington stressed, confusion in the succession of antagonistic reflexes would involve "not merely inaccuracy at the outset of each new reflex, but would mean mutual destruction of the two reflex effects." [30]

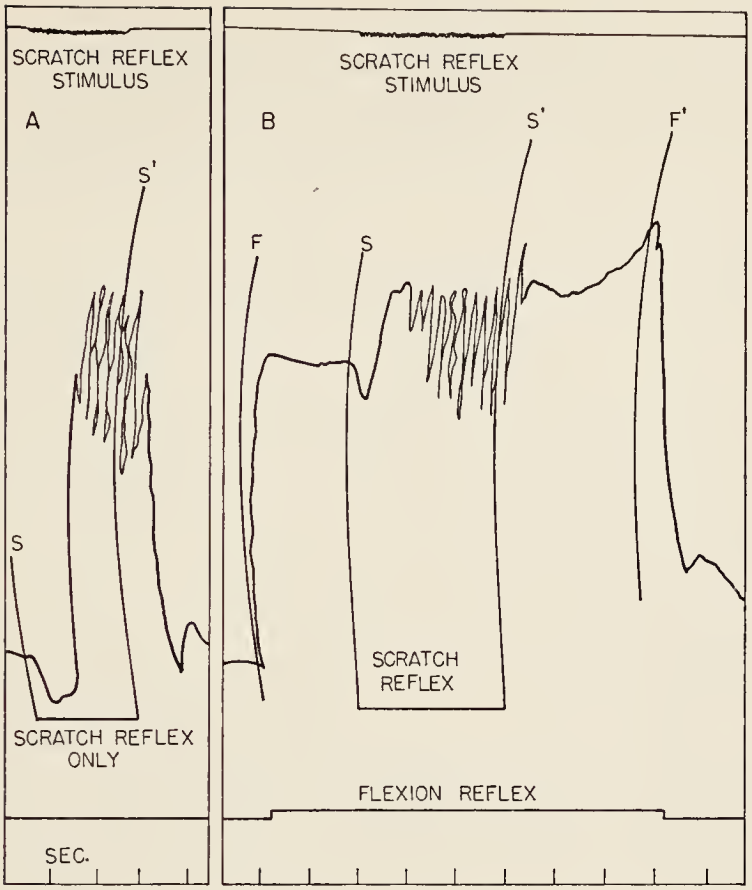

Fig. 13. *Successive Combination of Antagonistic Reflexes* (*scratch and flexion*). Effect of overlapping in time of the stimuli for the flexion-reflex and the scratch-reflex. Records from above downwards are:

Signal line: stimulus for scratch-reflex (*A* and *B*).

Myograph curve: in *A*, the vertical arcs indicate onset (*S*) and cessation (*S'*) of scratch-reflex stimulus only. In *B*, *S* and *S'* as in *A*; *F* and *F'* represent onset and cessation of stimulus for flexion-reflex.

Signal line: in *B*, ascent of lever marks stimulus for flexion-reflex.

Time in sec.

The scratch-reflex seems to displace the flexion-reflex; had it fused with it, the combined lift of the lever would have been much higher than it is. Compare the scratch-reflex in A and B.

In his study of reflex interactions Sherrington found that the time relations of stimuli of competing reflexes are a major factor determining the direction of an antagonistic sequence. The displacement of one antagonistic reflex by another, he discovered, may take several forms: inhibition succeeding excitation, excitation succeeding inhibition, or excitation of

one kind succeeding excitation of another kind — all forms of "interference." [31] The frequency of "interference" in reflex sequences effected by antagonistic succession, he commented, is very great. Two of the most important and common classes of such reflex sequences are "alternating reflexes" and "active compensatory reflexes." [32]

(3) *Reflex sequences.* The second half of Sherrington's sixth Lecture deals with the factors that determine the sequence of reflexes using a given common path. In view of the endless number of allied and antagonistic reflexes continually competing for possession of a common path, a knowledge of these factors, as Sherrington perceived, is a prerequisite for understanding the integrative action of the nervous system.

Sherrington delineated two groups of phenomena that underlie the resolution of reflex competition about a common path. First, and fundamental, are the "intimate" physiological processes effecting alliance and antagonism — summation and inhibition. Second, there is a cluster of four variables which largely condition the temporal sequence of reflexes over a common path: immediate or successive spinal induction, relative intensity of stimulus, relative fatigue, and the functional species of the reflex.[33]

All four of these variables, Sherrington held, can be resolved ultimately into *intensity of reaction.* Whether affected by stimulus species or intensity, fatigue or induction, those reflexes that are habitually prepotent are those that are habitually intense. He therefore saw each factor as "another agency working toward that plastic alteration of activities which is characteristic of animal life and increases in it with ascent of the animal scale" (p. 233).

Turning to the basic physiological processes of summation and inhibition, we have seen that Sherrington's own researches had done much to define their manifestations in reflex action.[34] Concerning their loci and possible modes of operation, he had (1) designated the internuncial neurone (common path) or motor neurone (final common path) of a reflex arc as the locus of summation; (2) proprosed that the synapse is the field in which "interference" or "inhibition" occurs; and (3) explained

reciprocal innervation by his hypothesis that an afferent fiber is duplex centrally, with specifically excitatory and inhibitory end fibers. In 1906, beyond citing his own data and hypotheses and reviewing other current ideas, Sherrington could do little more than offer a declaration of *ignormibus* about summation and inhibition: "As to the intimate nature of the mechanism which . . . by summation or by interference gives co-ordination where neurones converge upon a common path, it is difficult to surmise" (p. 143).

Despite his ignorance of the physiological or physicochemical bases of summation and inhibition, Sherrington showed definitively that their end result — an orderly sequence of simultaneously and successively combining reflexes — is essential for the integrative action of the nervous system. His fourth through sixth Lectures made clear the fundamental importance of "the principle of the common path" — the traffic routes for reflexes in the synaptic nervous system.

Using the striking analogies found in his 1904 address, Sherrington ended his sixth Lecture by enunciating the coordinative actions of the common path in phrases that bear repetition (the following quotations are taken from *The Integrative Action,* pp. 234–235).

> As a tap to a kaleidoscope, so a new stimulus that strikes the receptive surface causes in the central organ a shift of functional patterns at various synapses . . . The grey matter may be compared with a telephone exchange, where from moment to moment, though the end-points of the system are fixed, the connexions between starting points and terminal points are changed to suit passing requirements, as the functional points are shifted at a great railway junction.

Vastly more complex functional shifting is seen if one extends the principle of the common path from the relatively simple level of spinal reflexes to the whole animal, embracing the great receptors of the head and the complex neural circuits of the brain. "Releasing forces acting on the brain from moment to moment shut out from activity whole regions of the nervous system, as they conversely call vast other regions into play." In the action of these releasing forces, guiding the operations of

the spinal machinery, Sherrington saw the highest expression of the integrative action of the nervous system: *"The resultant singleness of action from moment to moment is a keystone in the construction of the individual whose unity it is the specific office of the nervous system to perfect."*

THE "PURPOSE" OF REFLEX ACTIONS

With the closing words of his sixth Lecture Sherrington moved from the relatively simple nature of coordinative or integrative reflex action at the spinal level to the complexities of integrative action in the whole animal, directed by the brain. His seventh Lecture, "Reflexes as adapted reactions," serves as a bridge between these two levels of analysis.

Sherrington had often turned his thoughts to the "purpose" or role of reflex actions in the animal economy, and his interest in this theme is not surprising.[35] First, of course, the study of a reflex's function bears on the understanding of motor coordination. He had seen, for example, that a reflex's "functional species" in part determines whether it will gain access to a common path: "reflexes arising in species of receptors which considered as sense-organs provoke strongly affective sensation . . . prevail over reflexes of other species when in competition with them for use of the 'final common path' " (p. 232). Furthermore, his scientific career began in the years when Darwinian theory was being brought to bear on topics such as the Pflüger-Lotze debate over reflex "purposiveness." And, lastly, as he revealed clearly in his foreword to the 1947 issue of *The Integrative Action,* the role of reflex actions in the behavior of higher organisms bore upon one of Sherrington's most abiding interests — the relationship between mind and body.

Sherrington began his seventh Lecture by stating again why he favored an explanation of reflex "purposiveness" in Darwinian terms: that is, a reflex must be purposive in the sense of having an adaptive or survival value for the animal (pp. 236–238). He next observed that the study of reflexes as adapted reactions falls into two ranks. In the intact animal the complex interactions of simple reflexes throughout the nervous system

"are ever combined into great unitary harmonies, actions which in their sequence one upon another constitute in their continuity what may be termed the 'behaviour' of the individual as a whole" (p. 238). Secondly — and this constituted the major focus of Sherrington's own work — one may consider the less intricate "purposes" of type-reflexes in a spinal animal — in what is essentially "a machine in action" (p. 238).

Data for determining the purpose of a given reflex, Sherrington explained, comes primarily from the conditions attaching to the reflex reactions, such as the mode and locus of its adequate stimulus and the time relations and spatial form of the response (pp. 238–240, 250–252).[36] But however facilely such data may be itemized, he warned with the voice of long experience, "the assignment of a particular purpose to a particular reflex is often difficult and hazardous" (p. 240). Two paramount problems which he cited are the high variability of reflex reactions from observation to observation, and that bane of all investigators, spinal shock.[37]

In the last part of Lecture VII Sherrington took up a particularly "difficult and hazardous" facet of the study of reflex purposiveness: the nature of psychophysiological relations seen in "the bodily resonance of emotion." "That marked reactions of the nervous arcs regulating the thoracic and abdominal organs and the skin contribute characteristically to the phenomena of emotion [generated in the brain] has been common knowledge from time immemorial" (p. 257).[38] The nature of the linkage between visceral reactions and emotions was a subject of considerable debate to which Sherrington had turned his attention some years earlier. In his seventh Lecture he reviewed the data and implications of his 1900 paper, "Experiments on the value of vascular and visceral factors for the genesis of emotion." His study had been directed toward testing the then favorite explanation of the relationship between the psychical and physiological elements of emotion: the James-Lange theory that emotion is the *result,* not the cause, of bodily changes.[39]

For several months Sherrington observed seven young dogs which had undergone spinal and vagal sections, severing all

sensory connections from the thoracic, abdominal, and pelivc viscera, skin, and muscles to the brain. In no instance, he found, could any impairment of "emotional character" be detected: judging by their actions and facial expressions, the dogs continued to experience "joy," "anger," "displeasure," and "fear." Accordingly, he felt, the James-Lange theory was invalid and he was "forced back" to the hypothesis that the visceral reaction is secondary to the psychical.[40]

Sherrington also compared the reactions of his experimental dogs, whose motor pathways from brain to cord were intact, with a decorticate dog studied by Goltz. Apart from vocal and facial signs of anger or displeasure, Goltz's animal reportedly remained "totally indifferent" to its surroundings. Sherrington felt that both Goltz's observations and his own studies of decerebrate animals supported the view that emotion is primarily a cerebral reaction and illuminated the levels of psychophysiological control operative in the nervous system. "Fear, joy, affection," Sherrington wrote,

> seem . . . to demand higher nervous organization than does anger. Be that as it may, the retention of its expression by Goltz's dog indicates that by 'retrogradation' the complex movements of expression has in certain emotions passed into a simpler reflex act . . . The impulsive movement of a 'lower' . . . so-called 'animal' emotion, has in this case become an automatic reflex no longer necessarily combined with the psychical state from whence it arose, of which it is normally at once the adjunct and symbol . . . [In the decerebrate animal] no cerebral reverberation descends to prolong and develop further the protective movement set going as a spinal reflex. This contrasts strongly with the fairly normal course that the headward part of the reflex, after loss of its vascular and visceral field, runs. The difference argues that the reverberation from the trunk, limbs, and viscera counts for relatively little, even in the primitive emotions of the dog, as compared with the cerebral reverberation to which is adjunct the psychical component of emotional reaction (pp. 267–269).[41]

THE BRAIN'S ROLE IN INTEGRATIVE ACTION

The brain, as Sherrington indicated throughout the first seven Silliman Lectures, directs nervous integration in the normal

animal. His own varied studies of the brain's role in motor integrations dealt primarily with the cerebrum and cerebellum.[42] Reviewing these researches and the work of many other investigators in *The Integrative Action,* Sherrington considered first the reactions of the motor cortex: its similarities to, differences from, and interactions with spinal centers in producing reflex movements (Lecture VIII). Second, in Lecture IX, he crystallized his ideas about the cerebrum and cerebellum's functions as the "head ganglia" for integrative action, and offered a general conception of the neural architecture of the motor organism.

The motor cortex. Sherrington's studies of the anthropoid motor cortex may be seen in one perspective as the culmination of his first excursions into neurophysiology — the study of brain-cord connections and pyramidal degenerations he undertook with J. N. Langley in 1881–82. His "return engagement" with brain localization studies came in two phases. During 1901–1903 he and A. S. F. Grünbaum (later A. S. F. Leyton), his assistant at Liverpool, published five short papers on the primate motor area. A second series of seven papers, written in collaboration with F. W. Mott, E. Schuster, T. Graham Brown, and A. S. F. Leyton, appeared from 1911 to 1918. Apart from the difficulties inherent in the researches, the gap in publications apparently was due in part to Sherrington's dispute with Victor Horsley in 1884. Sherrington and Leyton's major paper, "Observations on the excitable cortex of the chimpanzee, orang-utan, and gorilla," appeared in 1917 after Horsley's death.[43]

During the 1880's, with the advance in techniques of electrical stimulation and ablation, a detailed knowledge of the motor cortex had begun to emerge from the now classic researches of men such as Horsley, E. A. Schäfer, F. Semon, W. G. Spencer, and F. Gotch.[44] The majority of these researches during the 1880's were based on the cortex of the common monkey, Macacus. Thus, as Sherrington commented, "it was an interesting step further" when Beevor and Horsley published on the more complex cortex of an anthropoid species, the orangutan, in 1890 (pp. 296–297). Their study was a starting point for Sher-

rington and Grünbaum's research and was the only one on an anthropoid species until Sherrington and Grünbaum's first paper in 1901.[45]

When Sherrington and Grünbaum began work on the anthropoid cortex, using the orangutan, chimpanzee, and gorilla, they found the work slow, laborious, and complex. Referring to the work on the chimpanzee brain in a letter of September 8, 1901, to Harvey Cushing, Sherrington noted that "it will be some time before I can get the thing put together in a connected story." Again, on June 8, 1902, he told Cushing that "the anthropoid work drags its slow way along." [46] No better insight could be gained into the course of Sherrington and Grünbaum's first studies than that offered by the candid letter which Sherrington penned to Dr. Mond, a supporter of their work, on November 18, 1901, the same month in which their first "preliminary communication" appeared.

Dear Dr. Mond:

You kindly asked me for some report of the research on the physiology of the anthropoid brain. I expected to have before now the "proof sheets" of a "preliminary communication" on it which my friend Dr. Grünbaum & I sent in to the R. Society in the summer. But the "proof" is not yet to hand. So let me in the meantime write you the general position of the matter.

The very first experiment — on a chimpanzee — yielded results not in accord with the accepted teaching on the localisation of the centres. We thought our own technique at fault. Fortunately through your generosity we had means to obtain more chimpanzees. These confirmed instead of confuting our first observations. You then gave us money to buy an "Orang-outang." This was especially important because it had been on the orang-outang that the only previous experiment on the subject had been made, namely by Professor Horsley, and it was upon that one previous experiment that the doctrine of the past twelve years had been based. We were a little surprised to find in your Orang results not confirmatory of Mr. Horsley's, but in agreement with our own other observations on the Chimpanzee.

We almost immediately later obtained the rare chance of acquiring a Gorilla. My friend Prof. Elliot-Smith, a recognized authority on the anatomy of the anthropoids had impressed on me the correctness of Owen's view that the Gorilla's brain is the nearest of all to that of man. We got the Gorilla & successfully explored the

whole of the cortex cerebri (except one small piece) of both hemispheres. It yielded results closely like those from Chimpanzee; the differences were matters of comparative detail — of practical importance it is true because of close analogy to man, & therefore very significant to the surgeon and physician.

We have since then acquired a chimpanzee of the same kind as "Sally" of the zoo: considered very intelligent. And we have also got & successfully explored a second "orang outang", in order to once more attempt to bring our observations into conformity with Mr. Horsley's on that species. This second animal has however simply confirmed and somewhat extended our results obtained from the first.

Besides *stimulation* we have experimented by removal of certain brain-regions. Thus we have removed the famous "speech centre" as known in man. This did *not* impair the vocal sounds used by our animal. Among other things the removal experiments discover in Chimpanzee nerve-paths in the spinal cord considered hitherto to be exclusively human. The cord is therefore anthropoid as well as the brain.

Also, not wishing to waste anything of such costly material, we have experimented with the blood & find it "anthropoid" in a very curious way too long to trouble you with now, but very significant for physiological & pathological chemistry.

In one way our work disappoints me, since it has been much occupied in dispelling notions which were erroneous. Before contradicting current belief we have felt it needful to repeat our observations over & over: this has cost much time & much precious material. But it is now satisfactory to know that our observations & technique were, from the first, reliable. But the clearing of the old doctrine has been partly at sacrifice of the more ambitious semi-psychological problems that I had hoped to attack earlier. Sureness even at expense of speed is defensible in such matters. Our expenses have been very heavy: your early help was a stirring encouragement: I do not think we should have started without it. Let me thank you again. . . .

I am afraid Professors Horsley & Gotch will feel disappointed at our being unable to confirm their earlier work: but the work as it stands will be a marked increase to knowledge of the brain; & practical medicine will be a gainer. Prof. Ferrier the pioneer of such work in this country is to preside at a meeting of the London Pathological Society next month where I have been invited to open with this work a conference on Cerebral Localisation.[47]

Our preliminary communication contains simply a bald statement of results — absolutely without controversial reference. We are now busy with the photographs etc. for our full paper.

With grateful thanks for your aid, & hoping to be able before long to verbally communicate our work.

I am most truly yours

Ch. S. Sherrington.[48]

The results of Sherrington and Grünbaum's 1901–1903 researches, embodied in their well-known maps of cortical motor points (see Fig. 14), formed the point of departure for the eighth Silliman Lecture.[49] After reviewing that data, Sherrington felt that it was natural next "to inquire whether reciprocal innervation is exemplified by the reactions from the cortex" (p. 280). Citing a number of studies, including his own work on the limb and eye muscles, he showed that reciprocal innervation indeed is present, but that the cortex is not essential to the reaction.

The discussion of reciprocal innervations from the motor cortex led Sherrington into the third and final section of Lecture VIII, a comparison of cortical and spinal motor reactions. He had found some broad differences between local spinal and motor cortex reactions, primarily with respect to their mode of initiation and function. Spinal reflexes, he observed, suggest four "fairly obvious" functions — locomotive, protective, procreative, and visceral — and "seem to refer to stimulation of noci-ceptive or sexual skin nerves, or visceral afferent fibres, as though initiated by these." Movements elicited from the motor cortex, on the other hand, "carry the significance of possible responses to tactual, auditory, or visual stimuli" (p. 305).

More significant than these differences, to Sherrington, was the discovery that "salient objective differences" between motor cortex and spinal reactions "are for the most part less clear than might at first be supposed. The general statement that the co-ordination is of a 'higher' kind in [cortical reactions] has doubtless truth, but it proves vague when details are demanded. A co-ordination though simple may yet be perfect . . . If by higher co-ordination be meant that larger groups of reflex systems are simultaneously thrown into — or out of — action under cortical excitation than in merely spinal reflexes, that is more probable" (p. 288).

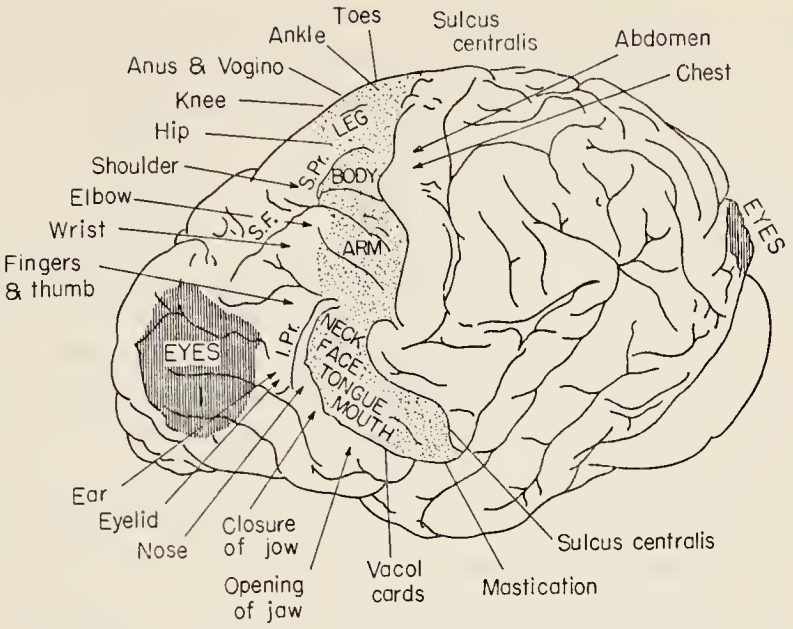

Fig. 14. *Cortical Motor Points* (from Grünbaum & Sherrington). Brain of a chimpanzee (*Troglodytes niger*). Left hemisphere viewed from side and above so as to obtain as far as possible the configuration of the *sulcus centralis* area. The figure involves, nevertheless, considerable foreshortening about the top and bottom of *sulcus centralis*. The extent of the "motor" area is hidden in sulci; for instance, the area extends into the *sulc. centralis* and *sulc. precentralis,* also into occasional sulci which cross the precentral gyrus. The names printed large on the stippled area indicate the main regions of the "motor" area; the names printed small outside the brain, indicate broadly by their pointing lines the relative topography of some of the chief subdivisions of the main regions of the "motor" cortex. But there exists much overlapping of the areas and of their subdivisions which the diagram does not attempt to indicate.

The shaded regions, marked EYES, indicate in the frontal and occipital regions respectively the portions of the cortex which, under faradization, yield conjugate movements of the eyeballs. But it is questionable whether these reactions sufficiently resemble those of the "motor" area to be included with them. They are therefore marked in verticle shading instead of stippling (as is the "motor" area).

S.F. = superior frontal sulcus. *S.Pr.* = superior precentral sulcus. *I.Pr.* = inferior precentral sulcus.

Sherrington pointed out two especially significant points of broad resemblance between motor cortex and local spinal reactions. First, reactions from the motor areas of a narcotized animal's two hemispheres, like those of a spinal animal's reflexes, fall into three groups: allied, antagonistic, and neutral.

Second, movements practically absent, such as bulbo-spinal reflexes, are also virtually absent from the cortex itself; conversely, movements regularly elicitable, like spinal reflexes, are liberally represented in the cortex.[50] This second point, Sherrington felt, "is striking, and yet is . . . not insisted on by writers" (p. 290).

Finally, Sherrington emphasized how the motor innervations active in decerebrate rigidity present a striking contrast to the groups of reflex movements elicitable from the spinal animal and the motor cortex. In brief, decerebrate rigidity, acting through the proprioceptive system and "some cranial mechanism seated between cerebrum and bulb, exhibits reflex excitation in those very groups of muscles which the local reflexes and the motor cortex when stimulated excite but little" (p. 301).

From the experiments and thought which produced this analysis of spinal, motor cortex, and decerebrate reflex actions Sherrington drew what was at the time a major conclusion about the production of motor coordination: the nervous system must have two separable systems of motor innervations, phasic and tonic, controlling two sets of musculature. "One system [cortico-spinal] exhibits those transient phases of heightened reaction which constitute reflex movement; the other [the system operative in decerebrate rigidity] maintains that steady tonic response which supplies the muscular tension necessary to *attitude*" (p. 302).[51]

Sherrington's analysis of the points of difference, resemblance, and interaction between motor cortex and spinal components of the phasic or reflex system yielded equally important insights into the types and levels of control needed for the integrative action of the nervous system. The spinal system, as he had shown in so many ways, can execute perfectly coordinated reflex actions. But with the motor cortex present and operative the extent and complexity of coordinated reflex actions is increased enormously, because the number of "neutral" or mutually indifferent reflexes possible in the body is greatly reduced. "This amounts to expressing concretely an inference that the cerebral cortex augments the motor solidarity of the

creature" (p. 306). With these words Sherrington was ready to discuss the final topic in his analysis of integrative motor action — the physiological position and dominance of the brain.

The head ganglia of the nervous system. Sherrington began his ninth and final lecture on reflex muscle management by restating certain key points from previous lectures, "in order to draw from them now in new juxtaposition some further significance" (see pp. 308–314, 319). The points, in sum, are those which distinguish the central nervous system of higher vertebrates from the diffuse nervous system of lower forms such as Medusa, and make possible the former's unique integrative action: (1) synaptically linked chains of neurones, (2) the afferent and efferent root cells which "form the pillars of a fundamental reflex-arch," (3) the coordinative mechanism attained by the principle of the common path, and (4) the "two great coordinative processes of *pluriceptive summation* and of *interference.*"

Following his reiteration of these essential points Sherrington turned to the nature of integration in the segment and segmental series. With the fore and aft (longitudinal) segmentation found in arthropods and vertebrates, he began, "the animal body has its first opportunity for really high differentiation" (p. 315). In a passage reminiscent of Pierre Flourens, Sherrington stated that the synaptic nervous system preserves functional unity amidst the body's segmental diversity in two ways. First, it "gives functional solidarity to the composite collection of unit lives and organs composing the individual metameres." Secondly, it welds the metameres together "into the unity of an animal individual" (p. 314).

Recognition of these two planes of functional unification, as Sherrington pointed out to his readers, opens the way to an analysis of the integrative action of the nervous system employing two sets of coordinates: (1) the individual segment, extended transversely across the body's longitudinal axis, and (2) the line of organs of analogous function scattered along the longitudinal segments. Nowhere did he demonstrate more fully

the fruitfulness of employing these two coordinates, singly and jointly, than in his account of the "physiological position and dominance of the brain" in integrative action.

He began his account by pointing out that the *receptor organs* which initiate reflex reactions in the nerve centers of each segment fall naturally into two main groups, distributed in three fields: (1) the deep or proprioceptive field, and (2) the surface field, consisting of exteroceptive and interoceptive regions (pp. 316–322). Through analysis of the intra- and intersegmental linkages afforded by the receptors' afferent spinal roots ("private paths") he proceeded to show how one may gain an "approximation" of the architecture of integrative action.

When the receptors are traced longitudinally (coordinate 2), as Sherrington had done in his Marshall Hall address of 1899 and his 1906 paper on the proprioceptive system, one finds that "remarkable developments" exist in the anterior or head segment. In Lecture IX he crystallized his concept of this segment's twin functions. Via two sets of receptors and "their ganglia" — the distance receptors and cerebrum and the labyrinth proprioceptors and cerebellum — the head segment drives the spinal apparatus and effects the coordination of phasic and tonic motor innervations.[52]

Two major points had emerged when Sherrington synthesized his researches on spinal reflexes and the functions of sensory nerves from muscles with current knowledge of the labyrinth cerebellar functions. First, he perceived that the labyrinth guides and interacts with the trunk and limb proprioceptors to originate and maintain tonic reflexes in skeletal muscle. "The labyrinth keeps the world right-side up for the organism by keeping the organism right-side up to its external world. The cranial receptors control the animal's *total* posture as do receptors of the hinder musculature the *segmental* posture of the hind-limbs when but the hind end of the spinal cord remains" (p. 341). Second Sherrington depicted the cerebellum, as "the head [or main] ganglion of the proprioceptive system." The cerebellum, by integrating the "afferent contributions from the receptors of joints, muscles, ligaments, tendons, viscera,

etc. . . . with those from the muscular organs of the head and with those of the labyrinth receptors themselves," ensures the coordination of postural reactions (pp. 346–347).

Although Sherrington gave due weight to the importance of the cerebellum and proprioceptive system for reflex muscle management, he judged that the brain's dominance in the integrative action of the nervous system is attained primarily by the operation of the distance receptors and their "head ganglion," the cerebrum.[53] This judgment, he felt, was bolstered by the views of comparative neurophysiologists. Their work, he stated, has indicated that the distance-receptors "have peculiar importance for the construction and evolution of the nervous system. In the higher grades of the animal scale one part of the nervous system has, as Gaskell insists, evolved with singular constancy a dominant importance to the individual. That is the part which is called the brain. *The brain is always the part of the nervous system which is constructed upon and evolved upon the 'distance-receptor' organs*" (p. 325).

To Sherrington a, or the, major function of the distance receptors in motor behavior is to initiate "anticipatory" or *"precurrent"* reactions. Such reactions, he maintained, work or control the animal's musculature *as a whole,* impelling movement or cutting it short by the assumption of a total posture (pp. 329–332).[54]

The ability of the distance receptors to initiate and guide motor reactions and thus to integrate the body segments into a functional whole, Sherrington saw, is due to the fact that their afferent arcs are "particularly wide and far-reaching," with two main channels of neural connections. First, their arcs have a "wide ramification . . . to the effector organs through the lower centers." Secondly, the distance receptors have "great connexions in the high cerebral centers. Briefly expressed, their special potency is because they integrate the animal through its brain" (p. 352).

For Sherrington no clearer revelation of the distance receptors' and cerebrum's dominance in integrative action could be gained than by observing a spinal or decerebrate animal, as he had done for so many countless hours.

The integration of the animal associated with these 'distance-receptors' . . . can be briefly with partial justice expressed by saying that the rest of the animal, so far as its motor machinery goes, is but the servant of them . . . By a high spinal transection the splendid motor machinery of the vertebrate is practically as a whole and at one stroke severed from all the universe except its own microcosm and an environmental film some millimeters thick immediately next its body (pp. 349, 351).[55]

In the course of this chapter I have attempted to conduct a "guided tour" of *The Integrative Action,* indicating the way in which Sherrington developed his analysis of reflex muscle management, his major conceptual statements, and the researches on which he based them. No single chapter can do justice to *The Integrative Action.* Its breadth and depth can be appreciated only by reading the work itself.

A reader of *The Integrative Action* will find, as I have tried to show, that the Silliman Lectures are a brilliantly constructed study, drawn from contemporary knowledge of vertebrate and invertebrate evolution, anatomy, histology, and physiology; above all, they encompass and crystallize the vast yield of Sherrington's first quarter-century of researches. Moving, step by careful step, from the nature of coordination in the simple reflex to the physiological dominance of the brain in motor behavior, Sherrington delineated the central premise of his concept of integrative action: "The nervous synthesis of an individual from what without it were a mere aggregation of commensal organs resolves itself into co-ordination by reflex action" (p. 7).

SHERRINGTON'S THREE LEVELS OF INTEGRATIVE ACTION

In the Silliman Lectures and in later writings Sherrington voiced distinct reservations about the ability of his concept of integrative action to account for the functional solidarity of vertebrates, especially among primate forms. Before appraising the integrative action concept as a watershed in the history of neurophysiology, we may end our study of its development by summarizing Sherrington's own assessment of its major factual and theoretical gaps.

Sherrington realized, first, that his concept left many questions about the nature of reflex motor control unanswered, and in the Silliman Lectures he stressed several sets of phenomena crucially in need of further definition. One set, dealt with in Lecture X, concerned the question of how volitional or conscious actions, actions connected somehow with the functions of the cerebrum, can interact with and modify the "intrinsic fatality" of reflex actions in higher vertebrates.[56] "It is," he wrote, "urgently necessary for physiology to know *how* volitional control is *operative* upon reflexes, that is, how it intrudes and makes itself felt upon the running of the reflex machinery . . . No exposition of the integrative action of the nervous system is complete, even in outline, if this control is left without consideration (p. 386).[57]

With regard to reflex mechanisms themselves, Sherrington saw that a complete theory of motor integration demanded a more detailed knowledge of such basic phenomena as synaptic inhibition and excitation. For this work, he realized, his relatively simple "input-output" methods would have to be supplemented and in time replaced by more sophisticated techniques and types of experiments.

Many new techniques, physiological, physical, and chemical, had been developed before Sherrington retired from Oxford's Wayneflete Chair in 1935.[58] In a 1936 letter to John Fulton he voiced his modest belief that the experimental yield of new methods, and the promise of their future harvest, largely had made the work embodied in *The Integrative Action* obsolescent. "Thank you for mentioning again that the old 'Integ. Act.' still floats. I know how generously you regard it, and am very grateful. But looked at rigidly I cannot but recognize that it has 'had its day.' Its best future is for what lives of it to be incorporated — unobtrusively — into what is written with a similar scope now and after for a time." [59]

Sherrington's last main cluster of reservations about the integrative action concept stemmed from his belief that reflex action was only a part, and a relatively small part at that, of the whole story of the integration of higher vertebrates. He himself might have written the words of the sixteenth-century

French physician, Jean Fernel, quoted in *Man on His Nature.* " 'Our task,' Fernel says, 'now that we have dealt with the excellent structure of the body, cannot stop there, because man is a body and a mind together' " (p. 136).

Fernel's words, indeed, epitomize the theme of Sherrington's Foreword to the 1947 reissue of *The Integrative Action,* an eleven-and-one-half page distillation of his years of study and thought about the roles and relationships of body and mind in animal integration. In the "Foreword" Sherrington distinguished three systems and levels of integrative action.

At the first level physicochemical processes weld the body's organs into a "unified machine," a welding exemplified by the integrative action of the nervous system. Sherrington's researches had been devoted to defining the nature of reflex action as the unit mechanism of nervous integration. But he emphasized, in 1947, that the Silliman Lectures should not be read as a statement that reflex motor behavior is "the most important and far-reaching of all types of 'nerve' behaviour." For, Sherrington asserted, "taken in comparison with the great field of behavior in general, pure reflex action of itself cannot be seen to cover such extensive ground as the instincts actuated by 'urges' and 'drives' " (pp. xv, ix, x).

Reflex action vanished completely as a mechanism in Sherrington's second system of integrative action, "the field of the psyche." At this level, he held, "the physical, creates from psychical data a percipient, thinking, and endeavouring individual." For Sherrington qua Cartesian dualist, "the physical is never anything but physical, or the psychical anything but psychical," yet the two systems "are largely complemental and life brings them co-operatively together at innumerable points." This mind-body liaison, to Sherrington, was the third and highest level of integrative action. "In all of those types of organisms in which the physical and psychical coexist, each of the two achieves its aim only by reason of a *contact utile* between them. And this liaison can rank as the final and supreme integration completing the individual" (pp. xv–xvi, xix).

To Sherrington, the "supreme philosopher of the nervous system," the most challenging and baffling problem for scientist

and philosopher alike was *how* the mind-body liaison is effected. In 1947, he commented succinctly, the issue "remains where Aristotle left it more than 2,000 years ago" (p. xix). It seems, as one reads Sherrington's writings on the mind-body relationship, that he was a dualist because it was for him the only tenable position in terms of scientific knowledge during his lifetime.

While Sherrington could offer no explanation of how the psychical and physical interact when considered as disparate entities, neither could he discover any valid bases for reducing mind to a manifestation of physical energy.[60] In view of this fact, as he explained in the closing sentence of the Foreword, dualism seemed to him as reasonable an assumption as monism. "That our being should consist of *two* fundamental entities offers I suppose no greater inherent improbability than that it should rest on one only" (p. xx).

When he was over ninety Sherrington made one of his final and most positive statements about the levels of integrative action that produce the totality of an animal such as man, and about the role of reflex action in that hierarchy. Said the author of *The Integrative Action,* during a conversation with Sir Russell Brain, "the reflex was a very useful idea, but it has served its purpose. What the reflex does is so banal. You don't think that what we are doing now is reflex, do you? No, no, no." [61]

VIII

"The Reflex Was a Very Useful Idea"

Each insight into mechanism reveals more mechanism still to know . . . But knowledge, while making for complexity, makes also for simplification.

NEUROPHYSIOLOGY'S WATERSHED

Studying the evolution of functional biology in general or a specialized discipline such as neurophysiology, the historian can perceive a recurring series of developmental stages and the interplay of several crucial variables. Since the time of Galen, who established a brain-nerve-muscle pattern of thought about how animals react to their environment, knowledge about the nervous system has developed through three often overlapping stages: recognition of gross anatomical and functional features, detailed study of gross and fine structure and of function, and detailed correlation of structure and function.

At least three interacting factors, in turn, appear to be vital for the development of and transitions between each stage. Examining the background to and contents of Sherrington's researches, for example, one sees the interplay among: (1) the types of techniques available to or developed by an investigator, (2) the necessity for a sound basis of anatomical knowledge on which functional studies can rest, and (3) the nature of the theoretical structure that an investigator brings to his work: the range and type of phenomena he seeks to define, and his interpretation of data, will be determined in part by whether his guiding theory or hypothesis was derived from extant empirical data in his field of study, or from another science, or from a metaphysic.

By the 1880's, as A. D. Ritchie suggested, the centuries-old development of data and theories about various structural and functional units of the nervous system presented a piecemeal state of affairs, reminiscent, as noted in Chapter II, of the oriental tale of four blind men examining an elephant. Controversy was rampant in almost every area of inquiry and, apart from some textbook presentations, few attempts had been made

to correlate structural and functional data within a given field of study, much less to interrelate the various separate channels of nervous system researches.

The study of reflex actions, for example, was pursued almost independently of concurrent work on problems such as the structure and interconnections of nerve cells, the differentiation of the spinal cord's sensory and motor functions, and the determination of brain structure and function. Within the field of reflexology itself, investigators such as Hall had discovered a vast number of specific reflexes and had begun to define the internal and external variables affecting their occurrence, such as the role of the stimulus. Experiments were in progress and theories being advanced, too, about some of the phenomena recognized as basic events in a reflex action, such as inhibition, excitation, and *Bahnung*.

A fairly extensive pool of techniques, data, and theories thus was available to a researcher in the last decades of the nineteenth century. But, as illustrated by the profusion of conflicting reports about the nature of the knee jerk, the whole field of reflexology was manifestly in need of restructuring. Techniques generally were imprecise, a sounder foundation of structural knowledge was needed, and, above all, there was a singular lack of experimentally based concepts with which to interpret the known facts of reflex action and evaluate their role in the animal economy.

The resolution of this piecemeal state of affairs was brought about, to an almost incredible extent, by the work of one man, Charles Scott Sherrington, over a period of twenty-five years. "The mission of Sherrington's life," John Fulton aptly states, "was the turning of anatomical facts of the nervous system into physiological language." [1] The success of Sherrington's "mission," as we have attempted to show in the course of this study, had many bases.

Two important elements were the nature of his scientific training and the men who influenced him most during its course. From his work in Michael Foster's laboratory at Cambridge and in the European laboratories of Goltz, Virchow, and Koch, he received a superb grounding in morphology and in

microscopy and its allied sciences of histology, pathology, and bacteriology. The way in which Sherrington chose to apply his training in and talents for morphology and histology was due, in large measure, to the influence of John Newport Langley and Walter Gaskell, under whom he worked at Cambridge. Langley and Gaskell shared a dominant interest, which they imparted to their student — how anatomical organization reflects, or is expressed in, physiological function. Thus, Sherrington had both the requisite scientific training and the mental set to accept Gaskell's suggestion that he concentrate his researches upon the physiology of the spinal cord. This facet of Sherrington's career has been summarized well by Granit:

> Sherrington, the trained microscopist turned physiologist . . . was ready at the starting-line when the great era of creative cellular histology began and problems concerning the structure of the central nervous system rose to actuality . . . he brought to the subject [of the physiology of the spinal cord] fresh insight into the necessity of knowing its cellular organization before further advance could be made.
>
> The nerve cell with its interconnections became his analytical unit. This was Sherrington's first great notion and one of his main contributions to neurology.[2]

In addition to his training and interest in histology Sherrington brought many other skills and personal qualities to bear on his study of the reflex functions of the spinal cord. The record of his published researches alone indicates Sherrington's abilities as an experimenter, from methodological design and the development of new techniques to the actual execution of an experiment. It is clear, too, that he came to his work possessed of four assets seemingly essential for truly creative scientific work: patience, a keenly observant mind, what Granit terms his "capacity for translating observation into problem," and a "synthetic attitude bent on emphasizing principles rather than *disjecta membra* of observation." [3]

The patience with which Sherrington approached each research problem is evidenced by his decade of "necessary preliminary steps" — the anatomical studies of motor and sensory pathways which he found often dull and pedestrian but essential for physiological work. The profusion of functional

studies that were generated by the anatomical work illustrate, in turn, Sherrington's observational powers and his ability to translate observations into research problems. These traits, coupled with his extensive grounding in the biological and medical sciences, endowed him with the ability to know what questions to ask Nature, how to ask them, and how to recognize the right answers. A statement by Sherrington, discussing the work of Jean Fernel and William Harvey, may be fittingly applied to his own career. "Essential to a great discoverer, in any field of Nature, would seem an intuitive flair for raising the right question. To ask something which the time is not yet ripe to answer is of small avail. There must be the means for reply and enough collateral knowledge to make the answer worthwhile." [4]

Sherrington's "flair for raising the right questions" led him into a vast, multi-faceted program of researches: brain-cord connections and spinal degenerations, the distribution of motor and sensory roots, the proprioceptive system, the characteristics of synaptic reflex-arc conduction, reciprocal innervation, the reflex patterns of the spinal, decerebrate, and intact animal, and the motor cortex.

By examining the antecedents to and tracing the course and content of these researches we have seen how strikingly the new outweighed the old in his work: in instance after instance Sherrington himself "made the time ripe" for answering a given problem. He pioneered new techniques and apparatus, such as the method of successive degenerations, surgical procedures for mammalian decerebration, the myograph, and the "electric flea," and established new methodological cannons with his meticulously designed and executed experiments. He marshaled and culled extant facts and theories and added a host of new ones about each topic he studied, always emphasizing in particular the correlation of structural and functional data.

The scope of his specific contributions clearly marks Sherrington as a major figure in the history of the neurosciences. The greater significance of his work, however, lies in his "synthetic attitude," in the fact that he perceived the interrelatedness of his varied researches. In his appraisal of Sherrington, Ragnar

Granit asks, "what motivated him? What was the vision he tried to reach?" [5] While Sherrington alone could have fully answered these questions, it seems clear that one of his goals was to explain the functional unity of motor behavior. At what point he set this goal, and at what point he realized that all his researches were pointing toward its attainment, are questions which again only Sherrington could answer precisely. From the contents of his 1897 Croonian Lecture on "The mammalian spinal cord as an organ of reflex action" it appears that he was moving toward the integrative action concept by that date. But it is difficult to know how much earlier he began to envision where his work might ultimately lead him, apart from a general aim of interpreting central nervous system functions in histological terms.

At least in retrospect, Sherrington's work from his first observations on the knee jerk in the 1880's through the publication of the Silliman Lectures in 1906 is resolvable into a three-fold study of reflex actions: their gross and histological architecture, the spinal and higher level mechanisms controlling them, and their functions in vertebrate motor behavior. From this study, using the nerve cell and its interconnections as his basic analytical unit, he in turn wove the revolutionary fabric of the concept of integrative action.

The idea of nervous integration, we have seen, did not originate *de novo* with Sherrington. The *fact* of motor coordination and the participation of the nervous system in its operation had been recognized since antiquity, and early prototypes of the integrative action concept are found in the ancient idea of "sympathy" on up through Flourens' studies of how specific brain regions affect an animal's functional unity. The uniqueness and significance of Sherrington's concept lies in the fact that it provided the first comprehensive, experimentally documented explanation of *how* the nervous system, through the unit mechanism of reflex action, produces an "integrated" or "co-ordinated" motor organism.

Thomas Kuhn's definitions of a "pre-paradigm" and a "paradigm"-directed science provide a suggestive model for appraising the field of neurophysiology in general, and the study of re-

flexes in particular, before and after the articulation of the integrative action concept. Kuhn defines a paradigm as a model embodying law, theory, and standards of methodology and application, "from which springs particular coherent traditions of scientific research." The "acquisition of a paradigm and of the more esoteric type of scientific research it permits," Kuhn believes, "is a sign of maturity in the development of any scientific field." [6]

A pre-paradigm scientific field, in contrast, is characterized by the lack of a research consensus. In the absence of a single generally accepted view about the nature of a given range of phenomena, Kuhn points out, various investigators confront the same data but describe and interpret them in different ways. The nature of fact-gathering in the absence of a paradigm, he holds, "creates the schools characteristic of the early stages of a science's development," each school shaped by an at least "implicit body of intertwined theoretical and methodological belief that permits selection, evaluation, and criticism." [7]

Placing the development of neurophysiology within a framework such as Kuhn's, I believe, supports and clarifies a central thesis of this study: the paramont importance of Sherrington's work from the 1880's to 1906 is the fact that it gave unified meaning to a host of phenomena and processes previously discussed in isolation. The concept of integrative action and all that it embodied brought together in a "final common path" many hitherto unconnected channels of neurophysiological, anatomical, and histological research.

By this unification Sherrington provided investigators of the nervous system with their first major paradigm, and concomitantly laid down fruitful guidelines that refashioned the course of their researches after 1906. It was this watershed achievement, synthesizing the work of one era and opening a new one, that led Sherrington's peers to designate him as "the main architect of the nervous system," "the supreme philosopher of the nervous system," "the author of the *'Principia'* of physiology," and the "man who almost singlehandedly crystallized the special field of neurophysiology."

"THE SHERRINGTON SCHOOL OF PHYSIOLOGY"

The scope of this monograph affords room merely to suggest, rather than document fully, how Sherrington's work refashioned the pattern of neurophysiological investigations in the twentieth century. Derek Denny-Brown has termed the enduring research traditions that sprang from Sherrington's Liverpool and Oxford laboratories "the Sherrington School of Physiology," and this "school" invites scrutiny from a number of perspectives.[8] Following Denny-Brown's lead, for example, one might make a "genealogical" study of the people and work that fed into and issued from the Sherrington school, and how the school's researches intersected other spheres of investigation in the neurosciences (see Fig. 15).

To those familiar with various branches of the neurosciences, the following list of names will provide some idea of Sherring-

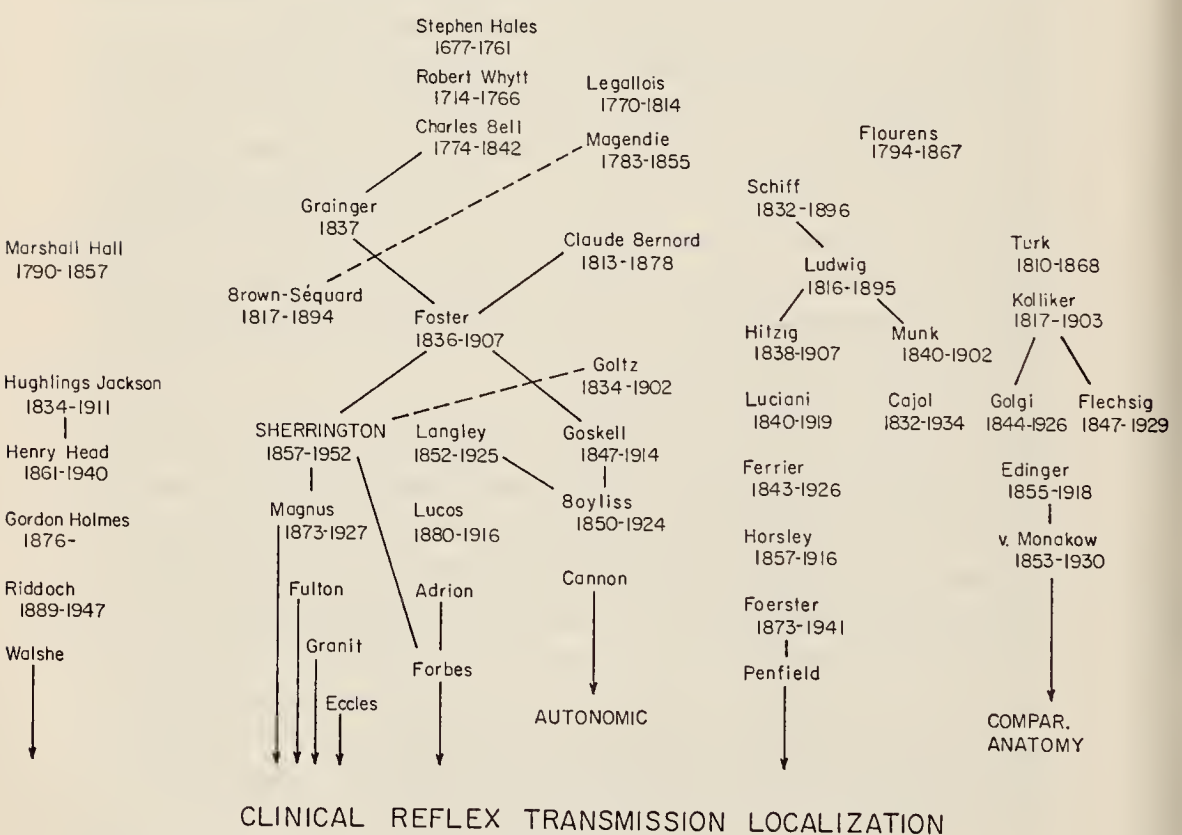

Fig. 15. *Constellation of neurological endeavor.*

ton's sphere of influence as both a teacher and a researcher. Among those who came to work under his guidance at Liverpool and Oxford were: H. C. Bazett, Lord Russell Brain, Stanley Cobb, Richard S. Creed, Harvey Cushing, Derek Denny-Brown, Nicholas B. Dreyer, Lord Florey, Alexander Forbes, John Fulton, William C. Gibson, Thomas Graham-Brown, Ragnar Granit, the brothers Ebbe and Hebbel Hoff, Gordon Holmes, Franc Ingraham, Sir Geoffrey Jefferson, David Lloyd, Ian Marcou, Karl Matthes, Grayson McCouch, Frederick R. Miller, S. Obrador, J. M. D. Olmsted, Wilder Penfield, R. W. Reid, David Rioch, H. E. Roaf, Theodore C. Ruch, K. Sassa, S. C. M. Sowton, Frances M. Tozer, Henry Viets, F. M. R. Walshe, Lewis Weed, and Robert S. Woodworth.

As the reader of Ragner Granit's book on Sherrington will discover, study of the Sherrington school and of the work of other neurophysiologists in the decades after 1906 shows the close association between the issues explored in *The Integrative Action* and the fruitful guidelines — methodological, empirical, and theoretical — that Sherrington provided for investigating them further. His experiments, we have seen, were never elaborate. He relied chiefly upon a blend of careful surgery, the use of modest electrical apparatus, and the meticulous correlation of structural and functional data.

Sherrington's methods may seem primitive to a contemporary neurophysiologist, whose sophisticated electronic and physicochemical techniques permit him to measure in tenths of milliseconds rather than in tenths of seconds and to analyze intracellular events within the "black box" of the central nervous system. The techniques that developed near the end of Sherrington's life, however, have not altered the graphic picture of reflex muscle management that he drew with his relatively simple "input-output" methods, and the fundamental pattern of his experiments established the framework for subsequent studies of the integrative action of the nervous system.

Short of delving into the past half-century of neurophysiological researches and duplicating Granit's study, the fruitfulness of the issues raised in *The Integrative Action* may be briefly illustrated by noting that they provided foci culminating in

three fundamental publications of Sherrington's Oxford period: his papers of 1924, 1925, and 1930 on the stretch reflex, central excitatory and inhibitory states, and the motor unit.[9] The work of Sherrington and his colleagues and pupils during 1913–1935 in turn formed the substrate for many subsequent major advances in unraveling the operations of the nervous system. For example, the analysis of the stretch reflex, which stemmed from Sherrington's observations on decerebrate tonus during the 1890's, led to the definition of the nature of autogenetic excitation and inhibition and hence to our present understanding of muscle tonus, attitude, and posture. Similarly, work on central excitatory and inhibitory states and the analysis of the motor unit culminated the research Sherrington had begun forty years earlier on the functional anatomy of sensory and motor pathways, and then led on to the study of the finer details of synaptic conduction that now fill volumes of textbooks, monographs, and journals.

Sir John Eccles, a member of the Oxford group and one of today's leading analysts of the structure and mode of operation of synapses, has written that "in almost every respect Sherrington's conceptual developments with regard to the synapse during the early decades of this century were on the direct path to the present position. So much so that the significant development of ideas can be very effectively illustrated by his writings." [10]

Broadening Eccles' statement, we may say that in almost every respect Sherrington's experimental and conceptual developments from the 1880's to 1906 were on the direct path to current views of the nervous system's integrative functions. His researches, *in toto,* showed how the reactions of the nervous system are explicable in terms of the behavior of synaptically linked neurones, each of which functions as a unit and exerts graded excitatory or inhibitory actions on other neurones, producing motor coordination by the unit mechanism of reflex action. Many of the fine details and implications of this schema of central nervous system activity came in the years after 1906, but while later work has added to the superstructure it has de-

manded little revision of the foundation set in *The Integrative Action.*

THE INTEGRATIVE ACTION CONCEPT AND EXPLANATION IN BIOLOGY

The course of neurophysiology before and after Sherrington's first quarter-century of researches reveals not only the modern worker's lineage from Charles Sherrington. It illuminates as well several trends characterizing the history of biology, particularly the ways in which biologists have approached the study of, and explained, the nature of living systems. The nature of explanation in biology has been part of a long controversy over how science can most fruitfully examine and account for the phenomena of living systems, a controversy extending at least from the time when Aristotelian teleology stood against the naive and speculative mechanism of the Greek atomists.

The question of how functional biologists have viewed the study of living systems and how their approaches have been reflected in the types of explanatory models they have constructed can, I believe, be explored fruitfully in terms of a proposal by Mendelsohn. The development of the biological sciences, he has suggested, is characterized by dual patterns of "unification" and "atomization" with regard to the study of given organs or systems, specific functions, or specific groups of living things.[11]

These dual patterns have been most evident in the nineteenth and twentieth centuries, which have seen, first, the emergence of a series of major unifying ideas about the nature of biological phenomena, such as the cell theory, Darwinian evolution, the milieu interieur concept, macro and molecular theories of gene action, and the integrative action concept. Secondly, at the level of direct and immediate causation, our knowledge of biological systems has been steadily reduced to smaller and smaller physicochemical components, a process of "atomization" that has engendered the interdisciplinary field of molecular biology.

To round out our study of Sherrington it is pertinent, I

believe, to indicate how "atomization" and unification operated in his work. By what approach and to what extent did he "atomize" the workings of the nervous system, and what level of explanation of biological phenomena does the integrative action concept represent? Or, casting the same general question in a somewhat different framework, we can ask what the integrative action concept tells us about the elements which enter into concept formation in the biological sciences. Is explanation in physicochemical terms or reduction to physical or chemical analogues essential in building up a new theory, or can one find strictly biological theories to explain biological phenomena?

In thinking about these questions I have found that Sherrington's work, experimental and conceptual, invites comparison with that of his noted French predecessor, Claude Bernard (whose pupils included Sherrington's own master, Michael Foster). Bernard, one feels, would have viewed Sherrington's investigations as an epitome of his dictum that "biology must borrow the experimental method of physico-chemical sciences, but keep its own special phenomena and laws." [12] For Sherrington, like Bernard, essentially approached his researches from a physiological position, never losing sight of the organism as a functional whole interacting with its environment.

We may, indeed, characterize Sherrington's classic investigations of vertebrate motor behavior by the statement that they were executed primarily on a *physiological level.* This, clearly, is not to say that he was unconcerned with the structural and physical-chemical bases of neural processes. As we have seen, he continually correlated anatomical and functional data, and he recognized that a full understanding of muscle management awaited determination of the physicochemical events responsible for inhibitory and excitatory synaptic action. His paramount concern, however, was to illuminate, not to "atomize," the complexity and interconnectedness of biological processes.

Faced with the question of how he could best analyze the operations of the nervous system, Sherrington chose in the vast majority of his experiments to study the input-output relations of reflex responses in the living animal, rather than the nature of isolated neuro-muscular phenomena *in vitro.* He sought to

define the workings of the nervous system in terms of *functional units,* such as the neurone-synapse, antagonistic muscles, the final common path apparatus, and simple and compound reflex patterns. These researches were accomplished, in essence, by making successive passages from the simple to the complex — a cyclical process which is one of the hallmarks of Sherrington's work.

Sherrington's "atomization" of vertebrate motor behavior thus seldom went beyond the level of histological units such as the nerve cell and its interconnections and physiological units such as the reflex arc and its operational properties. In time, he realized, other workers using other methods would further "atomize" the components he had defined, both at a physiological and at a physicochemical level, and by this reductionism shed more light on the integrative action of the nervous system. For, as he stated eloquently in his 1922 address on "Some aspects of animal mechanism," "Each insight into mechanism reveals more mechanism still to know . . . the elementary unit assumed simple proves, under further analysis, to be itself complex. Analysis opens vistas to further analysis required. But knowledge, while making for complexity, makes also for simplification." [13]

The experimentalists who have followed Sherrington would doubtless endorse Ragnar Granit's judgment that

> [his] greatest contribution to the physiology of the nervous system was to supply the functional equivalents of the anatomical [bases of neural organization]. His experiments led up to the functional unit, his concepts centered around unitary behaviour of cells activated or inhibited at synapses, and his 'integrative action' . . . is the knitting together of cells activated across synapses for a common goal . . . in the present era unitary analysis of nerve cells and their axons, pushed a second time to the frontier of research by Lord Adrian's work in the twenties and thirties, has given a richer harvest than any other approach to the physiology of the central nervous system.[14]

Sherrington himself, however, had a different evaluation of the primary significance of his work. His lifelong goal was to understand organized animal behavior. The biological importance of a reflex, he felt, is that it is a simple item of be-

havior, and through the study of reflex action he sought to uncover the basic elements fundamental to all coordinated, purposeful behavior.

The content and wording of the integrative action concept itself reflects Sherrington's essentially physiological approach to the study of the nervous system, and his preeminent "holistic" concern with the way that system functions in the animal economy. Physics and chemistry entered into the construction of the cencept primarily as they were used as methodological tools for obtaining data; physical or chemical processes, analogies, or models play little part in the actual content of the concept.[15]

The "holistic level" of Sherrington's explanatory model is revealed clearly by comparing one of his definitions of integrative action with those offered by two neurophysiologists writing in 1959.[16]

> The nervous synthesis of an individual from what without it were a mere aggregation of commensal organs resolves itself into coordination by reflex action.
>
> — Sherrington (1906)

> 'Integration' [may be defined] at an elementary level as comprising central facilitation, inhibition, after-discharge, spontaneity, modulation of pre-existing activity . . . Nervous integration [of this sort] is a function of synaptic junctions.
>
> — C. L. Prosser (1959)

> A large part of the remarkable flexibility of the central nervous system is determined by the fact that it develops not only excitatory, but also inhibitory synaptic activity. The special properties of these two electrically inexcitable components, interwoven in complex combinations by means of the conductile network that binds the activity of one cell to that of another exerts what Sherrington called the integrative actions [*sic*] of the nervous system.
>
> — H. Grundfest (1959)

Prosser's and Grundfest's definitions embrace the characteristic phenomena of reflex arc conduction which Sherrington explored in the context of his integrative action concept. But their statements, in striking contrst to Sherrington's, *nowhere mention the organism* in which and for whose "benefit" integrative action occurs. Passages such as theirs indicate, I believe, that modern investigators tend to atomize neural processes to the point where their biological setting often is forgotten. A similar

belief that modern investigators are in danger of neglecting the conceptual aspects of neurophysiological research has been voiced by Ragnar Granit as follows:

> In the present era one has the impression that electronic engineering has made the technical element 'foolproof' to the extent of attracting workers to this field who are ignorant of and uninterested in conceptual developments of the kind which the physiology of the central nervous system urgently demands. Sherrington's work should serve as a perpetual reminder of the necessity of long-range planning accompanied by ceaseless attempts to penetrate experiments and results with leading ideas.[17]

The development and content of the integrative action concept witnesses the fact that the explanation of biological phenomena may occur on at least two levels. On an operational or functional level a given phenomenon or system may be explained by distinctly biological concepts or laws, while at another level the same happening is analyzable into physical and chemical events. Since the seventeenth century the direction of biological research has been quite consistently unidirectional, hinging on work in the physicochemical sciences. Yet in the impact of Sherrington's analysis of the integrative action of the nervous system upon the neurosciences we see a striking example of the importance, if not the necessity, of distinctly biological concepts for understanding the nature of living systems.[18]

The power and fruitfulness of the concept of integrative action, I would thus suggest, derived in large measure from the fact that it was a distinctly biological and holistic construct. One of the most demanding tasks which the functional biologist faces is defining the workings of the nervous system, a system which in man contains over ten billion nerve cells and in which approximately three billion impulses are generated each second. Sherrington's work altered physiologists' orientation toward this most intricate of biological systems. For by his approach of reducing, for research purposes, the complex operations of the nervous system, analyzing it in terms of various structural and functional units, and building up again toward the role of reflex actions in the behavior of the organism as a whole, the nature of reflex action and its relation to nervous activity in general emerged in a new, more rational light.

Appendices

Sherrington's "Vital Statistics" [1]

"SHERRINGTON, Sir Charles Scott, O.M., 1924; G.B.E., cr. 1922: F.R.S.; M.A., M.D., D.Sc. (Cantab), F.R.C.P., F.R.C.S.; Hon. D.Sc., Oxford, Paris, Manchester, Strasbourg, Louvain, Upsala, Lyon, Buda Pesth, Athens; LL.D. London, Toronto, Harvard, Dublin, Edinburgh, Montreal, Liverpool, Brussels, Sheffield, Berne, Birmingham, Wales and Glasgow; late Wayneflete Professor of Physiology, Oxford; late Member of Medical Research Council of Privy Council; b. 27 Nov. 1857; m. 1892, Ethel Mary (d. 1933) y.d. of John Ely Wright, Preston Manor, Suffolk; one s. Educ. Caius College, Cambridge. Late Brown Prof. of Pathology, Univ. of London; Lecturer on Physiology, St. Thomas's Hosp., London; Royal and Copley Medallist and Past-Pres. of the Royal Society; Baly Gold Medallist, Royal Coll. of Physicians; Retzius Gold Medal, Royal Swedish Academy; Hon. Member Royal Irish Academy; Soc. de Neurologie, Paris; associate member of the Institut de France; member Imperial Academy of Medicine, Vienna; Foreign Member of National Academy of Sciences, Washington, French Acad. of Sciences, Real, Accadem. d. Scienze, Rome, and of Imperial Academy of Sciences, Petrograd; Royal Acad. of Medicine of Belgium and of Madrid; Member of Royal Acad. of Holland, Amsterdam; Royal Acad. of Sweden; Hon. Mem. Royal Danish Academy of Science, Copenhagen; Société de Biologie, Belge; Foreign Mem. Real. Accad. d. Scienze, Bologna; Hon. Fellow of Magdalen Coll., Oxford; Hon. Fellow Caius Coll., Cambridge; Hon. Fellow Roy. Soc. of Edinburgh; Hon. Member Physiol. Soc. of America; Soc. Medica di Roma; R. Accadem. di Scienze, Turin; Papal Academy Rome; Anglo-American Secretary, International Congresses of Physiology Liege, Berne, Cambridge, Turin, Brussels, Heidelberg; Vice-Pres. Brit. Child Study Assoc.; Pres. Physiol. Sect. Brit. Assoc. Cam. 1904; Dunham Lecturer, Harvard, 1927; Lister Oration, Canadian Medical Association, Toronto, 1927; Silliman Memorial Lecturer, Yale University, 1904; Page May Memorial Lecturer, University of London, 1910; Croonian Lecturer, Royal College of Physicians, 1913; Member of Board of Trade Committee of Sight Tests, 1910–12; Home Office Committee on Lighting of Factories and Workshops, 1913; War Office Committee on Tetanus, 1916–17; Scientific Com.

of the Central Board of Control, Alcohol, 1916–17; Professor of Physiology, Univ. of Liverpool, 1895–1913; Fullerian Professor of Physiology, Royal Institution of Great Britain, 1914–17; late Chairman, Industrial Fatigue Research Board, 1918; Nobel Laureate for Medicine, 1932; Gifford Lecturer, University of Edinburgh, 1936–38; a Trustee, British Museum. PUBLICATIONS: The Integrative Action of the Nervous System; Mammalian Physiology, 1916; School Hygiene (part author) 1913; papers to the Royal and other scientific societies, especially on the brain and nervous system; Selected Writings, 1939; Assaying of Brabantius, and other Verse, 2nd ed. 1940; Man on His Nature: the Gifford Lectures, Edinburgh, 1940, 4th ed. 1946; The Endeavour of Jean Fernel, 1946. ADDRESS: Gonville and Caius College, Cambridge. CLUB: Athenaeum."

Sherrington's Career at the Ipswich School

The following report on Sherrington's activities and achievements while a student at the Ipswich School was compiled by Wallace F. Morfey, a resident of Ipswich. Mr. Morfey undertook his researches at the request of Mr. Thomas D. Briden of the Ipswich School, whom I had written concerning Sherrington's career there, and transmitted his findings in the form of a letter to Mr. Briden.

20th May, 1965

T. D. Briden, Esq.,
34, Warrington Road,
IPSWICH.

Dear Briden:

I am sorry that such a great while has gone by before I have been able to get typed out the information which I found about Sir Charles Sherrington's School. As I suspected the local Press reported Speech Days almost verbatim in the 1870's, which includes the visiting examiner's reports, and I am pleased to say that in consequence I have been able to get together quite a fair picture of the course that the great man followed at Ipswich School.

It does undermine somewhat the oft repeated statement, which I believe originated from Rowley Elliston, namely, that Sherrington had a purely classical education at the School. It is undoubtedly true that it was predominantly classical, particularly in his earlier years in the lower forms, but, as will be seen, he was quite practised in other subjects as well. After all Mr. Elliston's information was not entirely contemporary, he being at the School from 1880 to 1887, whereas Sherrington left in 1876 before he ever came. I am sending you a copy of this letter as you may like to send this on to your correspondent who has enquired about this matter. I hope it is not too late for her purposes and will you please apologise to her for its very tardy arrival.

I might mention that in my searches in the local newspapers I worked backwards from the final years as I thought these would be more likely to mention Sherrington individually, and I will accordingly give the information now in similar sequence.

To begin with 1876 was a blank and it is clear, therefore, that he

must have left School at the end of the Easter term and so missed Speech Day in the summer.[2]

In 1875 he appears in the Prize List in several places. He won the Borough Members' prize for Modern History, the Headmaster's prize for English Verse, and the Cobbold prize for translation into English, and he got a 'Commended' in Mathematics and Arithmetic. The subject of the English Verse was "The Arctic Region", while the translation was from Euripides' Helen, verses 1526 to 1618. Unfortunately he does not get an individual mention as most of the rest of the Sixth Form did who were in specific sets, and it is clear, therefore, he was one of those who was working largely on his own and is covered by the examiner's following remarks: — "There are also on this (the Modern) side five boys who are preparing special subjects for various examinations, such as the R.M.A. at Woolwich, The Army Control Department, and the Legal and Medical Professions. These boys, although mostly superior I believe to the rest of the boys on the Modern side, did not come under my notice, their time being occupied in preparing for their respective examinations." As a matter of interest this particular examiner was The Reverend R. L. Howorth, grandson of Headmaster Howorth who presided over the School from 1800 to 1832.

In 1874 one of the examiners was The Reverend R. C. Whiting, an old Ipswichian and Sub-Warden of Radley College. In this year Sherrington was in the Upper Division of the Fifth, and another examiner comments on them saying that this Division "has prepared a part of the Odyssey of Homer. The translations of the five boys are vigorous and terse and their knowledge is good and well put. White, Baker, and Sherrington excel." Sherrington also appears in a report of a Mr. J. E. Taylor, F.L.S., F.R.G.S., who examined a number of boys in the Physical Geography examination. He was apparently pleased with them stating that the answers "are a much higher standard than I have hitherto experienced considering the short period over which the lectures on that subject extended. The papers on the advanced questions display a careful attention to the Lecturer's remarks and an intelligent appreciation of his chief points." In the list of marks Sherrington appears sixth out of the seven who are mentioned as being "of very high merit".

In 1873 he was, of course, in the Upper Fourth and the examiner was Professor Wilkins of St. John's College, Cambridge. He is mentioned in the following comments: — "The Upper Fourth Form acquitted themselves fairly in a viva voce examination in Homer's

Iliad 21–1, and the tenth book of Virgil's Aeneid, and very creditably in a searching Greek and Latin Grammar paper, in Latin prose composition and in the Greek in the Gospel of St. Matthew. Sherrington, Rawlinson, and Baker all did well in viva voce." In that year Sherrington won the High Steward's Prize for English Verse, his poem being entitled "Delphi", and this he recited at Speech Day, and he and Rawlinson shared the Classics and Divinity Prize in the Upper Fourth Classical side.

In 1872 he is again mentioned when the examiner says "the Lower Fourth Form with few exceptions were excellent; the work both on paper and viva voce was done with spirit and correctness. Rawlinson and Sherrington also deserve my commendation, and an English essay by Sherrington was unusually good."

I think that some remarks that the Headmaster, Dr. Holden, made in his report in 1873 sums up most completely the type of education through which Sherrington passed while in his hands at School here. The newspaper report of his speech is as follows:

"He believed the conviction was more and more gaining ground upon the public mind that the study of the Classics is the best possible instrument of education . . . In the system of classical education pursued at the School the powers of the mind were cultivated and strengthened, the memory exercised, and judgment trained, the power of analysis developed, the imagination fostered, and the understanding rendered more penetrating by the various processes which the youthful mind went through in learning a dead language.

"In the continued work of translation and re-translation a knowledge of our own tongue was gained, more accurate and more really useful than the mere study of English could convey. Besides this, grammar, which is the logic of common thought, was better learned in those languages of which the construction is more perfect. Latin and Greek were the basis of all modern grammar. Latin, moreover, was the best introduction to the study of modern languages. . . . At the same time he did not wish it to be understood that at this School they neglected the subsidiary subjects. They might be surprised to hear that in the Sixth Form, which he himself took, two days a week were entirely given to English Literature, so that it was quite evident that Classics could be pursued in a spirit more suitable to the requirements of the age than they were in former times."

An Experimental Protocol

The following protocol is a record of the first of five control experiments which Sherrington ran in his study of motor fibers in the monkey's lumbo-sacral plexus.[3] The protocol illustrates, first, the experimental methods which he used in his mapping of both motor and sensory pathways and, secondly, the meticulous, detailed records he kept of his investigations.

[In his control observations, Sherrington wrote,] the ventral nerve roots immediately above and immediately below the one to be investigated were divided; a sufficient time was then allowed for degeneration to have play; and finally electrical excitation of various nerve trunks in the limb was employed . . . Much of the motor defect at first resulting proves transient.

The numbers given indicate in centimetres the distance of the secondary coil on the slide of the inductorium; they are noted here merely to serve as a rough guide to the relative condition of the various nerves, and in comparing with one another the numbers for the opposite sides of the body and for the same side of the body, it is to be remembered that as the experiments progressed, the nerves, owing to exposure and other unavoidable causes, were some of them not in condition for accurately contrasting their excitability. Still the numbers appear to have a significance the broad features of which seem unmistakable.

[*Protocol I*]

25, vi. Young female. The 3rd and 4th and the 6th and 7th sub-thoracic roots of the right side divided completely just distal to the ganglion, i.e. ventral and dorsal divisions of the root severed together.

26, vi. Movements of right limb obviously impaired, seemingly less so at ankle than at hip and knee; the clasp of the right foot is feeble. Knee-jerk brisker right than left.

14, vii. Movements in cage seem almost normal; holds side of cage better with left hallux than with right. Continued observation detects performance at the hip of flexion, and extension; at the knee of flexion (outer hamstring

tightens very obviously both to inspection and to touch) and extension; at ankle, of flexion, and extension (latter weaker than left); in digits, of extension and flexion, latter weak.

10, viii. Obvious wasting of the anterior muscles of the right thigh, right calf, and of the inner hamstring mass. Knee-jerk is brisker right than left.

10.15 A.M. A.C.E. mixture administered; when anaesthesia has been obtained, anterior crural of right side is divided close below Poupart's ligament. Excitation of central end gives reflex on adductor group of the thigh.

10.42. Excitation of distal end gives extension at knee. Branches of anterior crural exposed and distal ends stimulated.

10.54. Upper branch to sartorius; no contraction.

Branch to rectus femoris — contraction at 15.
" " vastus externus and crureus — " " 19.
" " vastus internus and crureus — " " 16.
" " crureus — " " 18.

11.16. External popliteal close below gluteus maximus exposed. Central end gives reflex on to semimembranosus.
Distal end gives contraction in leg and foot.

11.28. Anterior tibial nerve. Distal end: contraction.
Musculo-cutaneous nerve. Distal end: contraction.

11.37. Distal ends of
a branch to tibialis anticus replies at 17. (Left side at 48).
a branch to extensor longus digitorum at 13. (Left side at 42).
a branch to extensor hallucis at 16. (Left side at 41).

11.53. Distal end of anterior tibial nerve on front of right ankle gives opening of toes with extension at 28 cm.
Distal end of same nerve left side at same place gives good opening of toes at 48 cm.

12.7. Right nerve to peroneus longus: contraction at 24 (left at 46).
Right nerve to peroneus brevis: contraction at 7 (left at 46).
(This result, not well in accord with my other experiments, was obtained in this experiment several times over at intervals during the experiments, being repeated in order to test its reality; although the figures obtained

varied somewhat the general features of the observation were constant, thus:

Peroneus longus at 12.11 = 27, at 12.33 = 25.
Peroneus brevis " " = 12, " " = 8.
at 12.48 = 24, at 1.14 = 22, at 1.15 = 23.
" " = 9, " " = 8, " " = 8.

Examined microscopically the nerve to brevis contained fewer fibres than nerve to longus).

Internal Popliteal.

12.35. Branch to external head of gastrocnemius, contraction at 23, (left at 49).
Branch to internal head, contraction at 30
" " soleus at 28 (left at 54).
" " tibialis posticus at 4 (left at 53).

12.55. Branch to flexor longus digitorum, feeble contraction at 26 (left at 48).
Branch to flexor hallucis at 21 (left at 57).

Hamstring nerve (3rd devision of Sciatic trunk).

1.17. Excitation of central end gives reflex.
" " distal end " contraction in hamstrings.
Branch to semimembranosus, contraction at 28 (left at 48).
Branch to semimembranosus, and adductor magnus, at 32 (left at 47).
Branch to semitendinosus, contraction at 25 (left at 49).
Upper branch to biceps, contraction feeble at 22 (left at 53).
Lower branch to biceps, contraction at 23 (left at 52).

1.54. Obturator nerve outside the obturator foramen.
Central end gave reflex on to psoas.
Distal end gave contraction in thigh.

1.59. Distal end of branch to adductor longus, contraction at 21.
Distal end of gracilis, good contraction at 24, but the upper part of the muscle is obviously wasted.
Branch to another part of the adductor mass, contraction at 18.
Branch to pectineus from anterior crural nerve, gives contraction feebly at 7, the muscle itself is obviously wasted.

On examination within the spinal canal it was found that the 5th root was intact, two roots above it and two below it being imbedded in fibrous tissue &c. When the dura mater had been opened it was found that excitation of the distal end of the divided rootlets of the 3rd and 4th and 6th and 7th nerves gave no detectable movement; excitation of the rootlets of the 5th nerve produced movement at the root of the tail. The 9th rootlets gave contraction in the tail. The 8th root was not excited because it was very adherent to the dura at one point.

The cord showed ascending degeneration to the naked eye even at the top of the cervical region, this degeneration proceeding from the dorsal root of the 6th lumbar chiefly, showing that the ganglion of the dorsal root of that nerve had been injured at the time of the first operation.

Table of Contents from Sherrington's 1898 Paper on Sensory and Motor Pathways[4]

II. *Experiments in Examination of the Peripheral Distribution of the Fibres of the Posterior Roots of some Spinal Nerves.* — Part II.

By Charles S. Sherrington, *M.A., M.D., F.R.S., Professor of Physiology at University College, Liverpool.*

Received November 12, 1896, — Read January 21, 1897.

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LONG INTRASPINAL REFLEX ARCS

Definition of the term

The main direction of spread is aboral, contrary to the 4th law of PFLÜGER

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Definition of the term

Sometimes symmetrical, but often, contrary to PFLÜGER's 2nd law, asymmetrical

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The Contents of Sherrington's Silliman Lectures[5]

YALE UNIVERSITY

Syllabus of Silliman Lectures for 1904,

By

PROFESSOR CHARLES S. SHERRINGTON, M.D., LL.D., F.R.S.,

OF THE UNIVERSITY OF LIVERPOOL

SUBJECT:

Integrative Action by the Nervous System

April 22, Friday.

Lecture I.

Physiological study of the integration of the animal body by the nervous system. Integration of a simple organism by the primitive nerve-net. The reflex unit: receptor, conductor, effector. Intercalation of the synapse into the conductor. The synaptic nervous system set over the nerve-net. Visceral and vascular innervation. Minute and precise use of time achieved by the nervous system: demand for this unequal in different parts of the organism: the synaptic system supplies it best.

April 23, Saturday.

Lecture II.

The synaptic system supplies isolated correlation between distant parts. Subdivision of effector organs and segmentation (metamerism). The segmental concept of the nervous system. The segments of a high type of vertebrate as judged by receptor and effector segmental fields. The nervous system of the segment. The integration of the segment as evidenced by nervous reactions. More minute and precise use of space given by

isolated correlation: yet the nervous system remains a continuum.

April 25, Monday.

Lecture III.

More varied use of space given by the synaptic system than by the nerve-net. With complexity of the organism increase in number and species of receptors means correlation to a greater variety of changes in a greater number of environment points. Reflex arcs and the principle of the common path. Successive use, not simultaneous use, of common paths permitted. The proprio-ceptive field. Its quota of receptors. Characters of its reflexes — maintained, secondary. Nervous background and transient reactions. Spinal inhibition of knee-jerk. The common path acts as a whole. Conflicting arcs. Central inhibition and peripheral inhibition compared.

April 26, Tuesday.

Lecture IV.

Common paths in relation to private paths. Centrality of the nervous system. The exteroceptive division of the surface field and its richness in receptors. Category of extero-ceptors. Skin pain: evidence of specific sense apparatus initiating it: characters of the reactions: nociceptive arcs, facile, protective. Nociceptive reactions prepotent in competition for common paths. Weak and strong reflexes. Reactions to which strong affective tone is adjunct are prepotent: such reactions, usually consummatory. Physiological incongruity of nerve-trunks: yet yield homogeneous results, because common paths interrelated.

April 28, Thursday.

Lecture V.

Seeming inequality of reflex facility of motor mechanisms in one and the same segment. The extensor stroke. Positive stereotropism. Reflex progression of the limb. Apaesthesia. Progression under decerebrate rigidity. Transient and maintained reactions. Forms of reflex contractions: brief, rhythmic, cataleptoid, maintained. Features of conduction referable to

grey matter: delay, irreciprocity, summation. Conditions determining prepotency over the common path — quality of receptor, intensity of stimulus, duration of reaction. Central fatigue.

April 29, Friday.

Lecture VI.

The "scratch" reflex: reaction compared with the cardiac refactory period: intensity, variation of form, two types of movement; the path of the arcs; proprio-spinal aboral tracts; the reflex plurisegmental and its arcs disynaptic with an internuncial path; fatigue and its place of incidence; attempt to obtain central fatigue; mutual reinforcement of allied arcs; the whole common path reacts as a unity; competition of conflicting arcs for the common path; two forms of central inhibition; after effects of inhibition. The common path a passive instrument in the hands of the various arcs. Distinct receptors and conjoined receptors; conflicting and allied arcs. Some psychical aspects of central interference.

April 30, Saturday.

Lecture VII.

Spinal shock. Shivering. Meaning of spinal reflexes. Pseudoaffective reflex, and its spinal path. The relation of visceral reactions to the coarser emotions.

May 2, Monday.

Lecture VIII.

Nervous integration of the segmental series. Refinements of the receptors in the leading segments. Restriction of distribution a factor toward integration. Distance receptors: their frequency of use; they drive the total animal: they imitate and guide precurrent reactions as contrasted with consummatory: germ of conation attaching to them: derive affective tint from consummatory reactions to which they lead if associative memory attach. The brain developed over the arcs of the distance receptors, i.e., the ganglion of the distance receptors. Relation between locomotion and receptive range. The "head" as physi-

ologically conceived. The head and trunk and internuncial paths. Severity of spinal shock proportionate to the so-called height of the animal's neural development.

May 3, Tuesday.

Lecture IX.

Physiological method and the functions of the cerebrum. The "excitable" cortex in dog, monkey, and anthropoid ape. Topography of places yielding reactions: strength of stimulus, epileptiform effects, primary and secondary movements: reinforcements, e.g., perineum and trunk, neck and ocular deviation. Narcosis depth. Reciprocal innervation experiments. Silence of the postcentral gyrus. Evidence of pyramidal tract. Character of the tract in anthropoids. Contrast in structure between precentral and postcentral cortex — cells, fibres. Degeneration consecutive to amputation, amyotrophy, and tabes dorsalis. Recovery of function after cortical ablation of limited extent. Hierarchy of centres.

May 4, Wednesday.

Lecture X.

Confluence of neural paths taken as token of psychical synthesis: tendency to accept also the converse. Convergence of retinal paths toward same region of cortex interpreted as indicating that synthesis of twin retinal impressions to a single sensation is effected by confluence to a single unitary neural mechanism. Binocular flicker. The rotating binocular lantern. Symmetrical flicker; asymmetrical flicker. Some uniocular and binocular comparisons. Binocular fusion in this case a time-combination, not a spatial combination. Cortical localization and composition of a sense-perception. Examination of anthropoid brain for a speech centre. Conclusion.

Sherrington on Sensory Integration and the Uses of Psychology

Sherrington's tenth and final Silliman Lecture dealt with the nature of sensual fusion in binocular vision and with the similarities and differences between sensory and motor integrations. He had built up an extensive collection of monographs on the psychophysiology of vision before he was thirty and remained well acquainted with the literature in the field.[6] In his 1937–38 Gifford Lectures he suggested one fundamental reason for his life-long interest in the nature of visual processes. "The first and greatest problem vision faces us with is doubtless that attaching to it as part of the mind-matter relation. How is it that the visual picture proceeds — if that is the right word — from an electrical disturbance in the brain?" [7]

Between 1896 and 1904 Sherrington published five papers on binocular vision, examining the perceptual result of presenting conflicting stimuli (flicker and contrast) to the two eyes.[8] It was this work, in a somewhat expanded form, that he presented in his last Silliman Lecture.

He began the Lecture by explaining the reasons for his apparently abrupt excursion from reflex muscle management into the field of subjective sensory phenomena. In brief, he felt that in seeking to trace the integrative action of the nervous system "it is natural to attempt to cross the gulf from movement to sensation." Whether sensations and feelings actually do accompany an animal's motor reactions, he acknowledged at the outset of his attempt, is an open question "to which the present time gives no clear answer." "But," he added, "we may agree that if such sensations and feelings or anything at all closely like them do accompany the reactions we have studied, the neural machinery to whose workings *they* are adjunct lies not confined in the nervous arcs we have so far traced but in fields of nervous apparatus that, though connected with those arcs, lies beyond them, in the cerebral hemispheres." [9]

In the intact animal the receptive points and organs which evoke reflex movements also initiate sensations. Like motor reflexes, Sherrington pointed out, these sensual reactions are of various grades of complexity and rest on a number of external and internal vari-

ables. The simple perceptual image of an object, for example, is usually the result of stimuli applied jointly to several sense organs: "the cigar taken from its box may be simultaneously sensed through eye and hand and nose and ear. The object [cigar] experimentally regarded as a single object excites a neural reaction that has its starting points in many spatially and qualitatively distinct receptive points, each point the commencement of separate nervous arcs." [10] Can we, Sherrington wanted to know, in any way compare the synthesis of the nervous elements whose combination underlies a simple sense perception with the simultaneous coordination of nervous factors in a motor reflex?

He approached this question about the nature of sensory integration much the same way he had the study of motor coordination: reduce the complexity of the phenomenon to a point where its variables are readily controllable. Using the cigar illustration, he observed that the complexity of the sense-percept can be reduced by limiting its paths of initiation to a single sense — the visual — excluding the *seen* cigar from directly stimulating olfactory, auditory, tactual, or muscular sense-channels. "Then we have left as regards the external stimulation merely the fusion of the right-eye and the left-eye images. This fusion is so complete that we cannot by introspection discriminate in the visual image [of the cigar] the right-eye image from the left-eye image. Moreover, this fusion is so elemental that . . . it appears innate." [11]

Simple and elemental as the *visual* percept of the "cigar" appears to be, it is a three-dimensional object with shadings of perspective and color and with characteristic associations. A sense-percept can be simplified further, as it was in Sherrington's experiments, by substituting for the "cigar" a simple and relatively meaningless discoid patch, of moderate, even, and uncolored brightness, and small enough to lie wholly on the central area of each retina.

His chief apparatus was an ingeniously designed rotating binocular lantern, with a light source arranged so that bright and dark phases could be made to occur simultaneously or alternately in conjugate retinal points of his subject's eyes. With this apparatus he sought, in essence, to provide a basis for comparing simple sensory and motor integrations by examining the nature of the tie between corresponding retinal points in perceiving asymmetrical and symmetrical binocular flicker and contrast.

As Lord Adrain commented in 1957, Sherrington's results "were clear enough but their interpretation was, and remains, puzzling,

for there is too wide a gap, too much unexplored territory, between the physical stimulus and the mental experience [of visual perception]." His data, in brief, seemed inexplicable by the generally accepted anatomical explanation of binocular fusion. When a subject perceives flicker and contrast, Sherrington reported, single vision with two eyes is *not* due to an anatomical confluence of the twin paths from corresponding retinal points.[12]

On the basis of his experiments Sherrington maintained, in contrast to accepted doctrine, that the convergence of the optic tracts from corresponding retinal halves to the same field of brain-cortex "does not signify physiological conjunction of right and left sense impressions." Rather, he held, the convergence of optic paths is a common path arrangment effecting the *motor* integration of conjugate eye movements.[13] *Sensual fusion,* he judged in turn, must somehow occur at a *"psychical"* or perceptual level.

> Were the nervous reactions initiated at twin points of the retinae *early* in its path along the retino-cerebral nerve-chain, to enter mechanisms common to both, there must, under 'alternate' or 'synchronous' right-left arrangement of stimuli, be interference, algebraic summation, etc., a coalescence of events which, though apsychical in itself, would involve subsequent confusion of the sense-reactions of the two eyes. A state of things wholly different from this is revealed in the results of our experiments . . .
>
> Our experiments show . . . that during binocular regard of an objective image each uniocular mechanism develops independently a sensual image of considerable completeness. The singleness of the binocular perception results from the union of these elaborated uniocular sensations. The singleness is therefore the product of a [perceptual] synthesis that works already elaborated sensations contemporaneously proceeding.[14]

Sensual fusion thus seemed to Sherrington strikingly different from reflex motor integration. The latter, as his researches had shown, rests in part on the principle of the common path — a "spatial confluence of the neural processes or mechanisms involved to a unit apparatus." In his binocular vision experiments, however, "contemporaneity of itself" seemed to suffice for sensual synthesis. The combination of left-eye and right-eye images, he wrote later in *Man on His Nature,* is "a temporal conjunction in 'mental' space . . . Identity in time and in perceptual space suffice. It instances the 'now' as an integrating factor of the finite mind." [15]

Sherrington's data, and his interpretation of them even more so,

were and remain at variance with accepted theories of visual processes. He recognized that his position "is one not generally admitted by physiologists or psychologists." But it was, for him, a position which permitted fruitful commentary about the apparently disparate natures of sensual and motor reactions, and one which he hoped might shed light upon the workings of "mind." [16]

As we have indicated, Sherrington saw no point in trying to explain sensual and perceptual processes in terms of the neural mechanisms which synthesize reflex movements. He granted that cerebral elements are extensively interconnected, and that this spatial conjunction must be important for the production of phenomena such as consciousness. But, he asserted in 1906, the "limitless postulation" of cerebral neural conjunctions "leads not so much to explanation of the high degree of unity of the individual mind as to an ultimate fallacy which Professor James has trenchantly termed that of 'the pontifical cell'. Pure conjunction in time without necessarily cerebral conjunction in space lies at the root of the solution of the problem of the unity of mind." [17]

Conversely, however, Sherrington believed that a knowledge of the characteristics of sensual reactions could help to resolve the nature of motor reactions. In his own work, for example, he had often described or defined reflex phenomena by an appeal to sensory phenomena (e.g., visual contrast and successive spinal induction, visual after-image and reflex after-discharge, and the use of psychological data for classifying the reflex-receptors and reflexes as adapted reactions).

Beyond the above points of contact between "the physiological and the psychical signs of neural activity" Sherrington saw another fact imperatively linking the psychological and the physiological for the biologist. In higher animals especially, he wrote, the "intrinsic fatality" of "pure reflexes" are controlled by higher centers.

> . . . the reactions of reflex-arcs are controllable by mechanisms to whose activity consciousness is adjunct. By these higher centres, this or that reflex can be checked, or released, or modified in its reaction with such variety and seeming independence of external stimuli that the existence of a spontaneous internal process expressed as 'will' is the naive inference drawn . . . It is urgently necessary for physiology to know *how* this control — volition control — is *operative* upon reflexes . . . No explosion of the integrative action of the nervous system is complete, even in outline, if this control is left without consideration.[18]

As one might expect from the foregoing passage Sherrington felt a need for and urged a rapprochement between psychology and physiology, and was deeply interested in psychology's scientific maturation. In the closing sentence of *The Integrative Action* he voiced his belief that "it is around the cerebrum, its physiological and psychological attributes, that the main interest of biology must ultimately turn." [19]

Two decades later, in a letter to John Fulton, he expressed his views on psychology's progress toward resolving the "psychical" functions of the cerebrum, and the ability of psychological and neurophysiological researches to aid each other.

> . . . it is a long step from spinal reflexes to 'dementia' psychosis! The whole eternal psycho-physical problem lies between! Psychological analysis has not reached yet a degree of simplicity of psychical unit comparable to that of the physiological units reached by physiological analysis: for instance, contrast 'a sensation' with a 'nerve impulse' (as unit reaction of conduction). Is is to me questionable whether psychology has as yet reached any even approximately 'elemental' psychical unit . . . Psychology has, I think, to analyze deeper before physiology can help it much.[20]

There is evidence that Sherrington himself hoped to advance the scientific level of psychological analysis and to bring psychology and physiology closer together by publishing a textbook of psychology in the late 1920's. The evidence rests on two statements by John Fulton. On December 31, 1926, he began a letter to Sir Charles with the following words: "I neglected in my last [letter] to ask you about your proposed textbook of psychology. I have been looking forward to this with keenest expectations. You wrote some time ago that the Cambridge University Press was printing it; is it now under way?" Ten months later, while Sherrington was in America to deliver the Dunham Lectures at Harvard Medical School, he visited the Fultons in New Haven. On October 12, 1927, Fulton wrote in his diary: "[Sir Charles] told me [today] of the progress of his new textbook of psychology which seemed to depress him from time to time and he puts it aside. Already, however, some 200 pages are written, but he considers the fundamental problem of the relation of mind to matter as insoluble, and he believes that psychology can only be approached profitably by admitting this at the outset." [21]

The psychology text apparently was never completed, and its

contents as well as the fate of the manuscript are unknown.[22] Thus, one can only speculate on how the master analyst of motor integration would have dealt with what he viewed as the second great integrative system of the organism: "the field of the psyche." [23]

Notes Bibliography Index

Notes

ABBREVIATIONS USED IN NOTES AND BIBLIOGRAPHY

Amer. J. Psychol.	American Journal of Psychology
Ann. Med. Hist.	Annals of Medical History
Ann. of Sci.	Annals of Science
Arch. Anat. und Physiol.	Archiv für Anatomie und Physiologie
Arch. Anat. und Physiol., Lpz.	Archiv für Anatomie, Physiologie und Wissenschaftliche Medicin. Leipzig
Arch. f. Psychiat. und Nervenkrankh.	Archiv für Psychiatrie und Nervenkrankheiten
Arch. f. Psychiat. Nervenheilk.	Archiv für Psychiatrie und Nervenheilkunde
Arch. gén. de méd.	Archives générales de médicine
Arch. Neurol. and Psychiat.	Archives of Neurology and Psychiatry
Beit. z. Anat. und Physiol.	Beiträge zur Anatomie und Physiologie
Brit. Assoc. Rep.	British Association Reports
Brit. J. Psychol.	British Journal of Psychology
Brit. Med. J.	British Medical Journal
Bull. Hist. Med.	Bulletin of the History of Medicine
Centralbl. f. Physiol.	Centralblatt für Physiologie
Deutsche Med. Wschr.	Deutsche Medizinische Wochenschrift
J. Hist. Med.	Journal of the History of Medicine
J. Neurophysiol.	Journal of Neurophysiology
J. Neurosurg.	Journal of Neurosurgery
J. Physiol.	Journal of Physiology
J. Physiol. expér. et pathol.	Journal de physiologie expérimentale et pathologique
Ludwig's Arbeiten Physiol. Anat.	Ludwig's Arbeiten Physiologie und Anatomie
Med. Hist.	Medical History
Med.-Chir. Trans.	Medical-Chirugical Transactions
Neurol. Zbl.	Neurologisches Zentralblatt
New Engl. J. Med.	New England Journal of Medicine
Obit. Notices Roy. Soc.	Obituary Notices of Fellows of the Royal Society
Pflüg. Arch. ges. Physiol.	Pflüger's Archiv für die gesamte Physiologie
Philos. Trans.	Philosophical Transactions of the Royal Society of London
Proc. Roy. Soc.	Proceedings of the Royal Society
Proc. Roy. Soc. Med.	Proceedings of the Royal Society of Medicine
Proc. Zool. Soc.	Proceedings of the Zoological Society
Psychol. Rev.	Psychological Review
Quart. J. Exptl. Physiol.	Quarterly Journal of Experimental Physiology
Sci. Monthly	Scientific Monthly

Sitzber. Akad. Wiss. Wien	Sitzungsberichte der matematischnaturwissenschaftlichen Classe der Kaiserlichen Akademie der Wissenschaften Wien
Ztschr. f. allg. Physiol.	Zeitschrift für allgemeine Physiologie
Ztschr. f. Biol.	Zeitschrift für Biologie
Ztschr. Rat. Med.	Zeitschrift für Rationelle Medizin.

PREFACE

1. John F. Fulton, "Sir Charles Scott Sherrington, O.M. (1857–1952)," *J. Neurophysiol., 15* (1952), 168.

2. *The Integrative Action of the Nervous System,* 1st ed. 1906, 2nd ed. 1947 (New Haven: Yale University Press Paperbound, 1961) pp. 2, 5.

3. The characterization of these two trends has been adopted from ideas expressed by Professor Everett Mendelsohn in a history of biology lecture at Harvard University, May 5, 1965.

4. Hebbel H. Hoff and Peter Kellaway, "The early history of the reflex," *J. Hist. Med., 7* (1952), 211–212.

5. As a matter of form, I have corrected occasional spelling errors contained in quotations from both published and unpublished material.

CHAPTER I. SHERRINGTON: THE MAN AND HIS JOURNEY

1. F. M. R. Walshe, "A foundation of neurology. *The Integrative Action of the Nervous System.* By Sir Charles Sherrington," *Brit. Med. J., 2* (1947), 823; Wilder Penfield, "Sir Charles Sherrington, poet and philosopher," *Brain, 80* (1957), 407.

2. E. G. T. Liddell, *The Discovery of Reflexes* (Oxford: Clarendon Press, 1960), p. v. Sherrington's son, Carr, wrote that "father's view was that a man should be judged by his achievements and not by what he looked like in his perambulator" (Personal communication, November 14, 1964).

3. Edgar D. Adrian, "The analysis of the nervous system: Sherrington Memorial Lecture," *Proc. Roy. Soc. Med., 50* (1957), 992.

4. For a fuller recital of Sherrington's honors see Appendix A. A lesser honor, his appointment in 1925 to the Medical Research Council, is worth recording for its announcement in the popular press. "The new member of the Medical Research Council, Sir Charles Sherrington, is one of the most famous scientists in the world. He discovered what is known as the 'autonomic nervous system' — the mechanism which enables the individual to walk and perform other automatic actions without the trouble of thinking." (*News of the World,* August 9, 1925.)

5. T. Graham Brown, "Sherrington: The man," *Brit. Med. J., 2* (1947), 810–812; Derek Denny-Brown, "The Sherrington school of physiology," *J. Neurophysiol., 20* (1957), 547.

6. Graham Brown, *Brit. Med. J., 2;* Penfield, *Brain, 80,* 408; Lord Cohen of Birkenhead, *Sherrington: Physiologist, Philosopher, Poet* (Liverpool: Liverpool University Press, 1958) p. 14; E. G. T. Liddell, "Charles Scott Sherrington, 1857–1952," *Obit. Notices Roy. Soc., 8* (1952), 257.

7. Alexander Forbes, Draft of a memorial tribute to Sherrington (Fulton papers).

8. R. S. Creed, "Obituary notice: Sir Charles Scott Sherrington," *Brit. J. Psychol., 44* (1953), 2; Statement made by Sherrington to Alexander Forbes (Fulton, Notes, 1921).

9. Draft of Sherrington Centenary Notice for the Royal Society of Medicine (Fulton papers). Little information is available about James N. Sherrington. Cohen of Birkenhead stated that he was a country doctor (*Sherrington,* p. 1). Fulton, in undated notes, wrote, "Lady Sherrington told me . . . that Mr. James Norton Sherrington [was] a barrister, dilettante, and Mayor of Yarmouth." Carr Sherrington stated that "James N. Sherrington was always called Mr. and I have no knowledge that he was a Dr. either in law or in medicine . . . [He] was mainly interested in art and was a personal friend of J. B. Crone and other painters of the Norfolk [School], possessing some of their most famous pictures . . . I have no record of the year he died . . . I always understood my grandfather had been a Mayor of Yarmouth and his father before him about the time Nelson had his fleet based at Yarmouth" (Personal communication, December 28, 1964). Carr E. R. Sherrington, *Memories* (by the author, 1957), p. 3.

10. Carr Sherrington, *Memories,* p. 2; Personal communication, December 28, 1964.

11. See Appendix B for W. F. Morfey's compilation of Sherrington's work at Ipswich.

12. Carr Sherrington, *Memories,* p. 2. Sherrington's devotion to Keats is illustrated well by a skirmish that occurred when he was seventy-two. At dinner one evening he "bristled up in righteous indignation" when a tutor in English literature, who considered himself an authority on poets, made some disparaging comments about Keats. For the next ten minutes the "combatants" recited yards of poetry, until the tutor had to back down after having been placed "skillfully and politely against a wall by Sir Charles" (Fulton, Diary, February 7–18, 1929).

13. See the Ipswich School examiner's report for 1875 in Appendix B.

14. Fulton, Diary, February 20, 1930; Personal communication, December 28, 1964; Sir Samuel Wilks (1824–1911), a physician and surgeon, served at Guy's Hospital, London from 1856 to 1911. He was a specialist in morbid anatomy and clinical medicine.

15. I have not been able to obtain information about the exact dates and nature of Sherrington's work at St. Thomas's and Edinburgh. Most of St. Thomas's records were destroyed during World War II (Personal communication from F. A. Tubbs, Hospital Librarian, December 28, 1964). According to D. H. Wood, Senior Administrative Officer at the University of Edinburgh Medical School, "there is no trace of Sherrington having matriculated as a medical student at Edinburgh between 1872–1882" (Personal communication, February 2, 1965). Carr Sherrington, *Memories,* pp. 3–4.

16. Vol. II (1713–1897), p. 446.

17. Carr Sherrington, *Memories,* pp. 3–5; his proficiency in languages is cited by Creed, *Brit. J. Psychol. 44,* 2. Apart from the note in Caius'

Biographical History, the College has "no record of Charles Sherrington's life or teaching" (Personal communication from Philip Grierson, College Librarian, October 30, 1964). Carr Sherrington similarly is unable to find any records of his father's work at Cambridge (Personal communication, December 28, 1964).

18. Edward Sharpey-Schafer, *History of the Physiological Society during Its First Fifty Years, 1876–1926* (London: Cambridge University Press, 1927), p. 25.

19. Fulton, Notes, March 4, 1936.

20. Graham Brown, *Brit. Med. J., 2.*

21. Sherrington, "Marginalia," in *Science, Medicine and History,* ed. E. A. Underwood (Oxford: Oxford University Press, 1954), II, 545. Sir George Murray Humphrey (1820–1896) became in 1842 the youngest hospital surgeon in England with his appointment to Addenbrooke's Hospital, Cambridge. He served, too, as Professor of Anatomy and then of Surgery at Cambridge. Sir George Edward Paget (1809–1892) introduced the first regular clinical examinations for the M.D. degree in England. He served as Bursar of Caius, Linacre Lecturer in Medicine at St. John's, and Regius Professor of Physic at Cambridge. J. N. Langley (1852–1925) entered St. John's College in 1871 and began attending Foster's classes in 1873. He succeeded H. Newell Martin as Foster's demonstrator in physiology in 1875. His study of the drug pilocarpine under Foster led him to a fifteen-year investigation of various exocrine secretory processes. From 1890 to 1906 he analyzed the origin and route of each sympathetic ganglion in the nervous system. He succeeded Foster as Professor of Physiology at Cambridge in 1903. Walter H. Gaskell (1847–1914) attended Foster's lectures while a student at Trinity College, studied medicine at the University College Hospital, and in 1883 became a lecturer in physiology at Cambridge. The bulk of his researches, dealing with the sympathetic nervous relations governing visceral organs, are summarized in his book, *The Involuntary Nervous System* (1916). Arthur Sheriden Lea, M.A., Sc.D., F.R.S. (d. 1915), was a Fellow and lecturer in physiology at Gonville and Caius College, a lecturer at Trinity College, and a University Lecturer at Cambridge.

22. Sherrington, "Marginalia," p. 545.

23. Quoted in Liddell, *Obit. Notices Roy. Soc., 8,* 243.

24. David Ferrier and Friedrich L. Goltz, "Discussion on the localization of function in the cortex cerebri," *Transactions of the International Medical Congress, 1* (1881), 228–233, 237–240. (Reprinted as "Neurosurgical classic XXII," *J. Neurosurgery, 21* [1964], 724–733.) Friedrich Leopold Goltz (1834–1902) studied physiology with Helmholtz and successively served as Professor of Physiology at Königsberg, Halle, and Strasbourg. David Ferrier (1843–1928) received his M.D. from Edinburgh in 1868 and joined the staff of King's College, London, in 1871, where he was appointed to a specially created chair of neuropathology in 1889.

25. The reader interested in work on localization of brain functions may consult the works by Gall and Spurzheim, Flourens, and Soury in the bibliography. Sherrington's later research on this subject will be discussed in Chapter VII.

26. Some of the committee's findings were reported in a series of papers in *J. Physiol., 4* (1883–84), 231–236.

27. Fulton, Notes (undated); J. N. Langley and C. S. Sherrington, "On sections of the right half of the medulla oblongata and of the spinal cord of the dog which was exhibited by Prof. Goltz at the International Medical Congress of 1881," *J. Physiol., 5* (1884), vi; Fulton, *J. Neurophysiol., 15,* 168.

28. The exact time at which Sherrington decided upon a career in pathology and the bases of his decision are unknown (Carr Sherrington, Personal communication, December 28, 1964).

29. Sherrington, "Marginalia," pp. 546–547.

30. Fulton, Notes, April 23, 1929.

31. The account of Sherrington's stay in Strasbourg is derived from Fulton's Notes, December 24, 1928 and Diary, October 23, 1927, and from Carr Sherrington's *Memories.* During his year at Strasbourg, Sherrington became well acquainted with J. R. Ewald, then Goltz's second in command, and with Jacques Loeb, fourth assistant to the master.

32. Everett Mendelsohn, "The emergence of science as a profession in nineteenth century Europe," in *The Management of Scientists,* ed. Karl Hill (Boston: Beacon Press, 1964), pp. 18–21. For a further discussion of the teaching-research orientation of German physiology and comparisons with France and England see the works by Ben-David, Fleming, and Merz in the bibliography.

33. Sherrington, "On secondary and tertiary degenerations in the spinal cord of the dog," *J. Physiol., 6* (1885), 177–191.

34. Quoted in Liddell, *Obit. Notices Roy. Soc., 8,* 243. As quoted by Liddell, Goltz's words were, "habe ich in ihm einen ebenso glucklichen Beobachter als uberaus geschickten Experimentator schätzen gelernt."

35. Fulton, Notes, December 24, 1938; Fulton, *J. Neurophysiol., 15,* 170.

36. C. S. Roy (1854–1897), a physiologist and pathologist, was Physician-Superintendent of the Brown Institution from 1882 through 1884, and in 1884 was appointed to England's first professorship in pathology, at Cambridge. J. Graham Brown (d. 1925) was an eminent Edinburgh physician; he devised various types of physiological apparatus, and did researches with Roy on capillary circulation.

37. Sherrington, "Marginalia," p. 548; Fulton, Notes, undated. C. S. Roy, J. Graham Brown, and C. S. Sherrington, "Preliminary report on the pathology of cholera Asiatica (as observed in Spain, 1885)," *Proc. Roy. Soc., 41* (1886), 173–181.

38. C. S. Sherrington, "Note on the anatomy of Asiatic cholera as exemplified in cases occurring in Italy in 1886," *Proc. Roy. Soc.* (1887), 474–477. His activities in Italy are mentioned by Carr Sherrington, *Memories,* p. 6 and by Fulton, Notes, December 26, 1928 and Diary, May 7–21, 1922.

39. Carr Sherrington, *Memories,* p. 6. The German pathologist Rudolph Virchow (1821–1902) was a Professor of Pathological Anatomy at Würzburg and at Berlin. In his 1858 *Cellularpathologie* he established the fact that every morbid structure contains cells which are derived from pre-existing cells. In his later years, Virchow turned from pathology to politics (he served as a liberal member of the Reichstag from 1880 through 1893), to anthropology, and to archaeology.

40. Carr Sherrington, *Memories,* p. 6.

41. Fulton, Notes, December 26, 1928. Robert Koch (1843–1910) is often described as the founder of medical bacteriology. His many fundamental contributions included new methods for culturing, staining, and identifying bacteria. He is known best, perhaps, for his 1882 discovery of Bacillus tuberculosis, a discovery which earned him the Nobel Prize in 1905.

42. Sherrington, "Marginalia," p. 549. Koch's remark, if Sherrington recounted the incident accurately after so many years, is a surprising one. In his classic paper of 1876 on the etiology of an anthrax, Koch wrote, "[it] seems . . . probable, that death [from anthrax] is due to a metabolic product produced by the parasite through its utilization of proteins as nutrients, and that this metabolic product is poisonous to the animal" ("Die Aetiologie der Milzbrand-Krankheit, begründet auf die Entwicklungsgeschichte des Bacillus Anthracis," *Beiträge zur Biologie des Pflanzen, 2* (1876), 277–310. Quoted from "The etiology of anthrax, based on the life history of *Bacillus anthracis,*" in *Milestones in Microbiology,* trans. and ed. T. D. Brock (Englewood Cliffs, N.J.: Prentice-Hall, 1961), p. 91.

43. Fulton, Notes, November 30, 1929 and December 26, 1928. Commenting on this incident in *Man on His Nature* (Cambridge: Cambridge University Press, 1941), Sherrington wrote, "for a classroom to exhibit an isolated brain-cell and label it large 'The organ of thought' may be dramatic pedagogy; it is certainly pedagogical overstatement" (p. 268).

44. Sherrington, "Marginalia," p. 549. According to Liddell, Sherrington mistakenly believed that his age, thirty, disqualified him from the Indian Medical Service (*Obit. Notices Roy. Soc., 8,* 244).

45. Sherrington, "Marginalia," pp. 552–553.

46. The Brown Institution, which housed England's first pathology laboratory, was founded with funds left to the University of London by Thomas Brown at his death in 1852. According to the terms of the bequest, the money was to be used for "the founding, establishment, and upholding of an Institution for investigating, studying, and . . . endeavouring to cure maladies, distempers, and injuries any Quadrupeds or Birds useful to man may be found subject to." If the institution were not founded within nineteen years, Mr. Brown stipulated, the money would go to the University of Dublin for professorships in languages. After deliberating for the full nineteen years, a University of London Committee and Trust opened the Brown Institution in 1871. Sherrington's predecessors as Professor-Superintendent were Sir John Burdon-Sanderson, founder of the pathology laboratory, Drs. Greenfield and C. S. Roy, and Victor Horsley (Lady Ghetal B. Burdon-Sanderson, *Sir John Burdon-Sanderson: A Memoir* [Oxford: Clarendon Press, 1911], pp. 80–83).

47. Account of the Sherringtons' life in London from Carr Sherrington, *Memories,* pp. 5–7.

48. Sherrington's stay in Paris was sometime in the 1880's (Carr Sherrington, Personal communication, December 28, 1965).

49. Sherrington, "Marginalia," pp. 550–551.

50. Quoted in Liddell, *Obit. Notices Roy. Soc., 8,* 244–245. Gaskell's influence may be seen by 1890 in Sherrington's papers on outlying nerve cells in the spinal cord; the papers record his attempt to find ganglion cells

at the periphery of the antero-lateral column of the mammalian cord as Gaskell had found in the alligator. Sherrington returned to this topic in his last scientific paper, published in 1940.

51. C. S. Sherrington, "Note on experimental degeneration of the pyramidal tract," *Lancet, 1* (1894), 265; polemic reply by V. Horsley, *Ibid.,* pp. 370–371; second note by Sherrington, *Ibid.,* p. 439; third note by Sherrington, *Ibid.,* p. 571. Victor Horsley (1857–1916) was an English physiologist and surgeon distinguished for his work on localization of brain functions and brain surgery. He served as Fullerian Professor at the Royal Institution from 1891 through 1893, and as Professor of Pathology at University College, London from 1893 through 1896.

52. Fulton, *J. Neurophysiol., 15,* 173.

53. Carr Sherrington, *Memories,* pp. 10–11. Sherrington's love of sports involved him in two accidents in 1908. The first, falling through thin ice while skating at Christmastime, caused no serious effects, but the second had lasting repercussions. While roller-skating at a rink in Liverpool, Sherrington, who was left handed, fell and broke his left arm. The arm mended slowly, and was frequently troublesome, especially when he later developed arthritis.

54. Carr Sherrington, *Memories,* pp. 5, 11–12. That the Sherringtons' interests did not always coincide has been reported delightfully by Fulton: "When Sir Charles retired from his chair at Oxford in the summer of 1935 at the age of seventy-eight, I happened to be there the day he was cleaning out his desk. In the back of a spacious drawer, covered up with papers, there were some fifty-eight medical incunabula which he explained, rather sheepishly, he had kept there because 'Dear Ethel' . . . hadn't fully sympathized with his interest in expensive books" (*J. Neurophysiol., 15,* 176).

55. Carr Sherrington, *Memories,* p. 10.

56. Fulton, Diary, May 7–12, 1922.

57. For an account of the Congresses see Kenneth J. Franklin, "A Short History of the International Congresses of Physiologists," *Ann. of Sci., 3* (1939), 241–335.

58. The University of Liverpool has no record of Sherrington's courses or pupils while he held the Holt Professorship (Personal communication, January 7, 1965). Sherrington's publications relating to his university and government work from 1902 to 1913 are listed in the bibliography.

59. The testimonials are quoted in Liddell, *Discovery of Reflexes,* p. 126.

60. Quoted in Fulton, *Harvey Cushing: A Biography* (Springfield, Ill.: Charles C Thomas, 1946), pp. 196–197.

61. Denny-Brown, "Charles Scott Sherrington," *Amer. J. Psychol., 65* (1952), 476.

62. Carr Sherrington, *Memories,* p. 12. Fulton, Diary, January 25, 1930.

63. Henry Viets, "Charles Scott Sherrington, 1857–1952," *New Engl. J. Med., 246* (1952), 981.

64. Fulton papers.

65. "Observations with antitetanus serum in the monkey," *Lancet, 2* (1917), 964–966.

66. Carr Sherrington, *Memories,* p. 13; quoted from Alexander Forbes, "The laboratory reacts," *Atlantic Monthly, 118* (1916), 544.

67. Liddell, *Obit. Notices Roy. Soc., 8,* 256. Some of Sherrington's researches at Oxford will be discussed briefly in Chap. VIII. For a detailed picture of his work during the Oxford years, see Ragnar Granit's *Charles Scott Sherrington: An Appraisal* (London: Thomas Nelson and Sons Ltd., 1966) and Sherrington's own *Reflex Activity of the Spinal Cord* (Oxford: Clarendon Press, 1932). *Reflex Activity,* written with R. S. Creed, D. Denny-Brown, J. C. Eccles, and E. G. T. Liddell, is an excellent summary of Sherrington's work after *The Integrative Action.*

68. Liddell, *Obit. Notices Roy. Soc., 8,* 256. Adrian is quoted in Cohen of Birkenhead, *Sherrington,* p. 12.

69. E. N. da C. Andrade, "Sir C. Sherrington, O.M.: A master of language," London *Times* Obituary Notices, March 7, 1952. For discussions of Sherrington as a poet see Carr Sherrington, *Memories,* Cohen of Birkenhead, *Sherrington,* Lecture III, and Penfield, *Brain, 80.*

70. Fulton, Diary, November 23, 1929.

71. Sherrington and J. C. Eccles, "Numbers and contraction-values of individual motor-units examined in some muscles of the limb," *Proc. Roy. Soc., 160B* (1930), 326–357. The Nobel Prize was awarded to Sherrington principally for the work reported in this paper.

72. Fulton, *Harvey Cushing,* pp. 606–607.

73. Granit, *Charles Scott Sherrington,* p. 98.

74. *Ibid.,* p. 99.

75. Letter from Sherrington to H. Cushing, June 15, 1933 (Fulton papers).

76. Carr Sherrington, *Memories,* p. 14; "Pope honours three Britons," *The Daily Telegraph* (London), October 31, 1936.

77. Cohen of Birkenhead, *Sherrington,* p. 64; Sherrington, *The Brain and Its Mechanism* (Cambridge: Cambridge University Press, 1933), pp. 22–23. Sherrington's views on the mind-body relation certainly were not shaped *de novo,* and suggestive comments may be found in works such as *The Integrative Action* and his 1922 address on "Some aspects of animal mechanism." In the latter, for example, he stated that "to pass from a nerve-impulse to a psychical event . . . is, as it were, to step from one world to another and incommensurable one" (*Brit. Assoc. Rep.,* 1922, p. 9). For a detailed exploration of Sherrington's dualism see Gösta Ekehorn, *Sherrington's "Endeavour of Jean Fernel"* and *"Man on His Nature"* (Stockholm: Acta Medica Scandinavica, Vol. 135, Supplement 231, 1949).

78. Penfield, *Brain, 80,* 409; *Man on His Nature,* 2d ed. rev. (Cambridge: Cambridge University Press, 1951), Preface. Much of the book was formed around the thoughts of Jean Fernel, the sixteenth-century French physician. Sherrington's long study of Fernel culminated in a scholarly biography, *The Endeavour of Jean Fernel,* published in 1946.

79. Quoted in Liddell, *Obit. Notices Roy. Soc., 8,* 258.

80. Letter, January 7, 1941 (Fulton papers).

81. Quoted in a letter from Ethel Davis to Mrs. John Fulton, November 27/28, 1939 (Fulton papers).

82. Sherrington was not a Catholic himself, though many of his family had been (Carr Sherrington, *Memories,* p. 15).

83. In 1942 he delivered the Phillip Maurice Lecture at Oxford, pub-

lished as *Goethe on Nature and Natural Science. The Endeavour of Jean Fernel* was published in 1946, and in 1947 he contributed a new preface for a reissue of *The Integrative Action.* A second edition of *Goethe* was edited in 1949; in 1950 he wrote the introduction for a series of broadcasts on "The Physical Basis of Mind"; and, in 1951, he re-edited *Man on His Nature* and added to it, as his final credo, a new chapter, "On Altruism."

84. Quoted in Cohen of Birkenhead, *Sherrington,* p. 15.

85. *New Engl. J. Med., 246,* 481.

CHAPTER II. AN ORIENTAL TALE: PRE-SHERRINGTON STUDIES OF REFLEX ACTION

1. A. D. Ritchie, "Sherrington as philosopher," *Brit. Med. J., 2* (1947), 812–813.

2. The "animal" in animal spirits was used in the sense of the Latin *anima* or "soul."

3. Descartes' theory of bodily automatisms was set forth in his posthumously published *De Homine* (1662), published in French two years later as *L'Homme.* In other works he expressed his equally influential philosophy of dualism: man is elevated above a mere machine by virtue of his immaterial rational soul, which interacts with the material body at the brain's pineal gland. Perhaps the most important figure in seventeenth-century nerve-muscle physiology was Jan Swammerdam (1637–1680), whose fundamental experiments are described in his posthumously published *Biblia Natura.* He developed the first frog nerve-muscle preparation, and with it tried to bring both voluntary and involuntary motion under a single neuromuscular principle. More than a century passed, however, before "spirits" and "sympathies" ceased to be major explanatory devices. In the eighteenth century, for example, J. B. Winslow's attempts to explain "sympathy" led him to coin the still-used term "sympathetic nerves." Seeing a structural resemblance between the ganglia of peripheral nerves and the brain, he postulated that the ganglia are small brains which can act as loci for nervous interactions. Thus, he said, the peripheral nerves are "sympathetic nerves" (*An Anatomical Exposition of the Structure of the Human Body,* trans. G. Douglas, 2 vols. [London: Prevost, 1733], Vol. I, Sect. 6, para. 364).

4. On the eighteenth-century divisions of experimental work see Mary Brazier, "The historical development of neurophysiology," in *Handbook of Physiology. Section 1: Neurophysiology,* ed. John Field, H. W. Magoun, and V. E. Hall (Washington: American Physiological Society, 1959), p. 11; the development of ideas about reflex action is discussed by Hebbel Hoff and Peter Kellaway, "The early history of the reflex," *J. Hist. Med., 7* (1952), 236, 239. Thomas Willis (1621–1673) was an English physician and pioneer neuroanatomist. In his 1664 *Cerebri Anatome* and his 1672 *De Anima Brutorum* he made many fertile suggestions about "involuntary" motions and localization of function in the nervous system.

5. Whytt's *An Essay on the Vital and other Involuntary Motions of the Animal* (1751) is the first known treatise dealing exclusively with what we

now term reflex action. His later studies of reflex action are described in his *Physiological Essays* (1755) and his *Observations on the Nature, Causes, and Cure of those Disorders which are commonly called Nervous, Hypochondriac, or Hysteric* (1764).

6. Johann Unzer, *Erste Gründe einer Physiologie der eigentitchen Natur thierischen Korper* (Leipzig: Wiedmanns, 1771); Jiri Prochaska, *De Functionibus Systematis Nervosi, et Observationes Anatomico-Pathologicae* (Prague: Gerle, 1784). Unzer's and Prochaska's treatises were translated into English by Thomas Laycock and published jointly by the Sydenham Society in 1851 (*The Principles of a Physiology of the Nature of Animal Organisms,* by Unzer, and *A Dissertation on the Functions of the Nervous System,* by Prochaska). Through Unzer's and Prochaska's writings, "reflexion" became an accepted and widely used word. Another advance in creating a language of reflexology was Unzer's coining of the terms "afferent" (*aufleitend*) and "efferent" (*ableitend*).

7. *The Functions of the Nervous System,* pp. 383, 429.

8. Denny-Brown, "The Sherrington School of Physiology," *J. Neurophysiol., 20,* 545–546.

9. Pierre Flourens, *De la Phrénologie et des Etudes Vraies sur le Cerveau* (Paris, 1863), p. 194.

10. Pierre Flourens, *Recherches Expérimentales sur les Propriétés et les Fonctions du Système Nerveux dans les Animaux Vertébrés* (Paris, 1824).

11. Sherrington, "The parts of the brain below the cerebral cortex," in *Text Book of Physiology,* ed. E. A. Schäfer (Edinburgh: Y. J. Pentland, 1900), p. 909.

12. Hall's description of a "reflex arc" is a prime illustration of his love for neologisms: "The anatomy of the diastaltic system consists in an esodic [afferent] nerve, the spinal centre, and an exodic [efferent] nerve, *essentially linked together,* and constituting a *diastaltic* nervous arc. The physiology of this system consists in such an arc or such arcs, in diastaltic action" (*Synopsis of the Diastaltic Nervous System* [London, 1850], p. 36). "Diastaltic" was a word Hall coined in an attempt to express the fact that impulses travel along the cord exciting reflexes in series.

13. Geoffrey Jefferson, "Marshall Hall, the grasp reflex, and the diastaltic spinal cord," in *Science, Medicine, and History,* ed. E. A. Underwood, II, 317.

14. *The Descriptive and Physiological Anatomy of the Brain, Spinal Cord and Ganglions, and of their Coverings* (London, 1845), p. 278.

15. Kölliker's *Handbuch,* published in 1852, was translated and published in English in 1853 (*Manual of Human Histology,* trans. G. Busk and T. Huxley [London: Sydenham Society]). Kölliker (1817–1905), a Swiss anatomist, physiologist, and embryologist, was a professor at Wurzburg from 1847–1902. His *Handbuch* was one of the first definitive histology textbooks.

16. The discovery of non-medullated fibers had been reported by the Polish-German physician Robert Remak (1815–1865) in his 1838 M.D. thesis at the University of Berlin. Kölliker, reversing the usual view, believed that nerve fibers are a separate tissue, *ending* rather than beginning in the nerve cells. Another notion advanced in the 1850's–1860's was

that nerve cells produce fibers as a sort of secretion, the connection severing when the fiber matured.

17. Account of Deiters' work from Brazier, "Historical development of neurophysiology," p. 26, and E. G. T. Liddell, *The Discovery of Reflexes,* pp. 22–27. Camillo Golgi (1843–1926) began his research on cells and tissues, particularly those of the nervous system, at the University of Pavia, and in 1880 assumed the University's chair of histology and pathology. His key discovery, the use of silver salts for selective staining, was made in 1873.

18. A. V. Waller, "Experiments on the section of the glossopharyngeal and hypoglossal nerves of the frog, and observations of the alterations produced thereby in the structure of their primitive fibres," *Philos. Trans., 140* (1850), 432; V. Marchi and C. Algeri, "Sulle degenerazione discendenti consecutive a lesioni della corteccia cerebrale," *Rivista Sperimentale di Freniatria, 2* (1885), 492.

19. Charles Bell, *The Nervous System of the Human Body as Explained in a Series of Papers Read Before the Royal Society of London* (Edinburgh: Black, 1836), p. 129. The basis of Bell's theory was his belief that muscles are supplied with sensory nerves which convey a "sense of the condition of the muscle" to the brain and are essential for regulating muscular action. Bell (1774–1842), a Scottish physician and surgeon best known for his work on the nervous system, began lecturing on anatomy and surgery in London in 1804. He became surgeon to Middlesex Hospital in 1812, senior professor of anatomy and surgery at the College of Surgeons in 1824, and was knighted in 1831.

20. Joseph von Gerlach (1820–1896) began practicing medicine at Mainz in 1850 and subsequently became professor of anatomy and physiology at Erlangen. He developed a number of important histological stains, such as carmine. Karl Wilhelm Ludwig (1816–1895), a German physiologist, was an influential teacher and researcher at Leipzig. His scientific contributions ranged from pioneer studies on glandular secretions to the development of a mercurial blood-gas pump that helped to define the role of oxygen and other gases in the blood. Rudolph Wagner (1805–1864) was a professor of physiology at Göttigen. Between 1842 and 1853, in collaboration with men such as Purkinje, Lotze, Ludwig, and Volkmann, he wrote a six-volume textbook on physiology and physiological pathology.

21. Liddell, *Discovery of Reflexes,* p. 89. The "all-or-none" law — that the contraction of a muscle fiber is always maximal — was demonstrated for heart muscle by Bowditch in 1871 and for skeletal muscle by Fick in 1882. In 1902 Francis Gotch showed that the nerve fiber also follows the all-or-none law.

22. J. von Gerlach, "Von dem Rückenmarke," *Handbuch der Lehre von den Geweben des Menschen und der Thiere,* ed. S. Stricker (Leipzig: W. Engleman, 1871–1872), Bd. II; Wilhelm His, "Zur Geschichte des menschlichen Rückenmarks und der Nervenwurzeln," *Abh. sächs. Ges. Akad. Wiss., 13* (1886), 477–513; August Forel, "Einige hirnanatomische Betrachtungen und Ergebnisse," *Arch. f. Psychiat. Nervenheilk., 18* (1887).

23. Sherrington, "Preface," in *Explorer of the Human Brain* by Dorothy F. Cannon (N. Y.: Henry Schuman, 1949), p. xiii. Account of Cajal's work

from Cannon, pp. 131–144, Sherrington, "Santiago Ramón y Cajal, For. Mem. R. S.," *Obit. Notices Roy. Soc., 4* (1935), 425–441, and Santiago Ramón y Cajal, *Recollections of My Life,* trans. by E. Horne Craigie, ed. in 2 vols. as *Memoirs of the American Philosophical Society* (Philadelphia, 1937), chaps. v–vii. Golgi's method, developed from 1880 to 1885, was designed to selectively and clearly stain nerve cells and nerve processes silvery-black. Although superior to other stains, which showed little more than cell bodies and nuclei, it was a lengthy and difficult process, hard to use successfully, and for a time was discredited.

24. H. W. G. Waldeyer, "Über einige neuere Forschungen im Gebiete der Anatomie des Centralnervensystems," *Deutsche Med. Wschr., 17* (1891), 1213–1218. Although Waldeyer is often mentioned as a founder of the neurone theory, his sole contribution was coining its name. Sherrington, a close friend of Cajal's, stated that Waldeyer's paper was published "without consulting Cajal" and "somewhat to Cajal's disgust" ("Preface," *Explorer of the Human Brain,* p. xii).

25. In 1906 Cajal and Golgi, somewhat ironically, shared the Nobel Prize "in recognition of their work on the structure of the nervous system." Cajal's Nobel address dealt with the "Structure et Connexions des Neurones"; Golgi, in turn, devoted a large part of his address, "La Doctrine du Neurone, Theorie et Faits," to an attack on the neurone theory (*Les Prix Nobels, 1904–1906.* Stockholm: P. A. Norstedt, 1907).

26. Ramón y Cajal, *Recollections of My Life,* pp. 336–337.

27. Brazier, "Historical development of neurophysiology," p. 27. Alexander Monro, for example, observed in 1783 that the spinal ganglia are formed on the posterior spinal roots and that a posterior root's coalescence with the anterior root is peripheral to this ganglionic "swelling." As had Galen, Monro held that the ganglia are concerned with "muscular nerves."

28. François Magendie (1783–1855), a French physiologist and physician, became Professor of Anatomy at the College de France in 1833. Magendie was one of the principal establishers of experimental physiology based on vivisection, a practice furthered by his foremost pupil, Claude Bernard. The contents of Bell's and Magendie's studies and their famous priority dispute have been detailed in J. M. D. Olmsted's *François Magendie* and G. Gordon-Taylor's *Sir Charles Bell.* In his 1811 *Idea of a New Anatomy of the Brain,* Bell stated that the anterior column and roots are *both* sensory and motor in function, while the posterior column and roots control the "secret operations" (autonomic) of the body's "vital" nerves. In 1822 Magendie, at the time unaware of Bell's memoir, stated that the posterior roots are primarily sensory and the anterior roots primarily motor in function. The priority dispute was ignited when Bell, in his 1824 *Exposition,* published altered versions of his 1811 memoir and 1821 Royal Society papers, changed to conform more closely with Magendie's 1822 report (see bibliography for complete references).

29. *Discovery of Reflexes,* p. 82.

30. Summary of Schiff's conclusions drawn from Liddell, *Discovery of Reflexes,* pp. 80–84.

31. 1st ed., 1877; 2d ed., 1878; 3d ed., 1879; 4th ed., 1880–1890; 7th ed., 1897 (London: Macmillan and Co.).

32. Leonard Landois, *A Textbook of Human Physiology,* 2d American ed., with additions by William Stirling (Philadelphia: P. Blakiston, 1887). First American ed., 1885. Based on Landois's *Lehrbuch der Physiologie des Menschen* (Wien: Urban und Schwarzenberg, 1880).

33. *A Textbook of Human Physiology,* pp. 654–669.

34. *Textbook,* 5th ed., III, 869–876. (Unless otherwise noted, further references to Foster's *Textbook* are from the fifth edition.)

35. *Textbook,* III, 880.

36. *Ibid.,* p. 886.

37. Landois and Stirling, *A Textbook of Human Physiology,* p. 657.

38. *Textbook,* I, 178.

39. *Ibid.,* pp. 182–183.

40. *Textbook,* III, 895, 896–897.

41. *Textbook,* 1st ed.; 5th ed., I, 78.

42. *Textbook,* II, 902.

43. *Ibid.,* 607; Landois and Stirling, *A Textbook of Human Physiology,* p. 661.

44. Landois and Stirling, *A Textbook of Human Physiology,* pp. 666–668.

45. *Ibid.,* pp. 661–663.

46. Unless otherwise noted, discussion of these four factors is from Foster, *Textbook,* III, 905–919.

47. Summation of stimuli had first been studied by Helmholtz in 1854 as the superposition of two electric shocks to skeletal muscle, termed by him "addition." Setchenov (1863) and Stirling (1874) took up the problems of summation in the spinal cord. By the 1880's it was known that sixteen feeble stimuli per second most effectively produce summation in the central nervous system, while induction shock stimuli are effective within much wider limits (0.05–0.4 per second). Stirling found too that the latent period between stimulus and response increases with fatigue, while Rosenthal (1873) and Wundt (1874) discovered that strong stimuli decrease latency (Landois and Stirling, *A Textbook of Human Physiology,* p. 662).

48. *Textbook,* III, 906.

49. Eduard Pflüger, *Die sensorischen Functionen des Rückenmarks der Wirbelthiere nebst einer neuen Lehre über die Leitungsgesetze des Reflexionen* (Berlin, 1853). Quoted in Landois and Stirling, *A Textbook of Human Physiology,* pp. 662–663.

50. *Textbook,* III, 909.

51. *Ibid.,* p. 911.

52. Landois and Stirling, *A Textbook of Human Physiology,* p. 664.

53. *Textbook,* III. 925 (Foster defined an "automatic action" as one resulting from "changes arising in the body or organ itself and determined by causes other than the influences of the circumstances of the moment" [p. 920]); Landois and Stirling. *A Textbook of Human Physiology,* p. 670.

54. *Textbook,* III, 918.

55. *Textbook,* I, 180–182.

CHAPTER III. A PRELIMINARY STEP: ANATOMICAL STUDIES (1884–1898)

1. Lord Cohen of Birkenhead, *Sherrington: Physiologist, Philosopher, Poet,* p. 26.

2. Sherrington, "On secondary and tertiary degenerations in the spinal cord of the dog," *J. Physiol., 6* (1885), 177–191. The term he introduced, which unfortunately has not endured, was "cord area" — the region of the cortex which is so directly connected with the spinal cord that lesions in the former induce degenerations in the latter. Studying the functions of the pyramidal tracts, he observed that the dog retains voluntary power after large destruction of both tracts: the animal can run and jump and only shows clumsiness in the execution of finer movements. Further, he noted, removal of the cord area first causes depression of the "deep" or tendon reflexes such as the knee jerk and then, after the second week, their exaltation on the side opposite the brain injury. A further report on his Strasbourg work appeared in 1890 ("Note on bilateral degeneration in the pyramidal tracts resulting from unilateral cortical lesion," *Brit. Med. J., 1,* 14).

3. "On nerve-tracts degenerating secondarily to lesions of the cortex cerebri," *J. Physiol., 10,* 429–432 (see also the two addenda in *J. Physiol., 11* [1890], 121–122, 399–400).

4. W. H. Erb, "Ueber Sehenreflexe bei Gesunden und Rückenmarkskranken," *Arch. f. Psychiat. und Nervenkrankh., 5* (1875), 792. C. I. O. Westphal, "Ueber einige Bewegungserscheinungen an gelähmten Gleidern," *Ibid.,* p. 803.

5. For example, Schultze and Furberger in 1875 abolished the jerk in rabbits by cutting the *n. cruralis* and Tschirijew in 1878 abolished it by cutting the cord between the 5th and 6th lumbar vertebrae. For a good summary and bibliography of work on tendon reflexes through the early twentieth century, see Franklin Fearing, *Reflex Action: A Study in the History of Physiological Psychology* (Baltimore: The William Wilkins Co., 1930; reprint, New York: Hafner, 1965), chap. xv.

6. The functional significance of the knee jerk was not fully recognized until the 1920's. Its seeming functional obscurity largely arises from the abnormal way in which the jerk is elicited. Through Sherrington and Liddell's analysis of the stretch or myotatic reflex, it was shown that the adequate stimulus for the jerk's reflex mechanism is a stretch of the muscle. In normal circumstances the stretch reflex is naturally imposed on muscles by the action of gravity, and is a crucial mechanism for the maintenance of posture and skeletal muscle tone.

7. A standard index of reflex time in the 1870's–1890's was Exner's measurement (1873) of the wink reflex in response to electric stimulation. Allowing for conduction time in the nerve and the time of muscle latency, Exner found that 55–47 milliseconds elapsed between stimulation of the right eyelid and movement of the left ("Experimentelle Untersuchung der enfachsten psychischen Processe," *Pflüg. Arch. ges. Physiol., 7* (1873), 601–660; *8* (1874), 526–537). While investigators obtained a wide range of values for the time of the knee jerk, they found, on the whole, values

as low as 2 milliseconds — far below Exner's time for a "pure" reflex such as the eye wink. The time argument continued to be advanced against the reflex interpretation of the knee jerk until 1910–11, when new galvanometric and photographic techniques showed that the jerk's stimulus-response time is long enough for reflex-arc conduction. For good summaries of the debate over the knee jerk at the end of the 1880's, see W. P. Lombard, "On the nature of the knee-jerk," *J. Physiol., 10* (1889), 122–148, and A. D. Waller, "On the physiological mechanism of the phenomenon termed the 'tendon reflex,'" *J. Physiol., 11* (1890), 384–395.

8. *Reflex Action,* p. 264.

9. W. P. Lombard, "The variations of the normal knee-jerk and their relation to the activity of the central nervous system," *Amer. J. Psychol., 1* (1888), 5–71. See bibliography for the Mitchell and Lewis, and Bowditch and Warren papers.

10. "Note on the knee-jerk," *St. Thomas's Hospital Reports, 21* (1891), 145–147. The observations on the monkey reported in this paper were later extended to the rabbit, cat, and dog ("Note toward the localization of the knee-jerk," *Brit. Med. J., 1* (1892), 545; "Addendum," *Ibid.,* p. 654).

11. Sherrington here found the anatomical basis for positioning a person's leg so that it hangs at a right angle to the thigh when testing the patellar reflex: the pose not only increases mechanical freedom of the leg at the knee joint, but also relieves the jerk of the normal physiological restraint imposed by the tension of the antagonistic flexor and hamstring muscles.

12. Sherrington, "Notes on the arrangement of some motor fibres in the lumbo-sacral plexus," *J. Physiol., 13* (1892), 621.

13. *Ibid.,* pp. 621–772. A preliminary report appeared in the *Proc. Roy. Soc., 51* (1892), 67–78.

14. D. Ferrier and G. Yeo, "The functional relations of the motor roots of the brachial and lumbo-sacral plexus," *Proc. Roy. Soc., 32* (1881), 12–20; Sherrington, *J. Physiol., 13,* p. 662. Unless otherwise noted the account of pre-Sherrington work on motor innervations is drawn from Sherrington's own detailed historical review (*J. Physiol., 13,* pp. 622–634).

15. C. Eckhard, "Über Reflexbewegungden vier letzen Nervenpaare des Frosches," *Ztschr. Rat. Med., 1* (1849), 281; J. Peyer, "Über die peripherischen Endingungen der motorischen und sensibelen Nerven wurzeln," *Ztschr. Rat. Med., 4* (1853), 67.

16. "The minute anatomy of the brachial plexus," *Proc. Roy. Soc., 41* (1886), 423–440.

17. The protocols of Sherrington's first five control experiments have been reproduced in Appendix C to illustrate the meticulous, detailed records he kept of his work.

18. Sherrington, *J. Physiol., 13,* p. 735. The German physiologist Johannes Müller (1801–1858) held professorships of physiology and anatomy at Bonn and Berlin. His many areas of research included the nervous system and comparative anatomy, and, as reflected by his influential *Handbuch der Physiologie des Menschen* (1833–1840), he was one of the main architects of modern physiology.

19. Sherrington first reported this observation in a paper, "The nuclei in the lumbar cord for the muscles of the pelvic limb," *J. Physiol., 13* (1892), viii-x.

20. *J. Physiol., 13,* p. 746.

21. *Ibid.,* pp. 747–748.

22. *Ibid.,* p. 663.

23. *Ibid.,* pp. 766–767.

24. The significance of his anatomical studies of sensory nerves in muscles for understanding motor coordination were detailed by Sherrington in the Silliman Lectures and his 1906 paper, "On the Proprioceptive System"; see Chapter VI.

25. Quoted in E. G. T. Liddell, *The Discovery of Reflexes,* p. 121.

26. "On the anatomical constitution of nerves of skeletal muscles; with remarks on recurrent fibres in the ventral spinal nerve-root," *J. Physiol., 17* (1894), 212.

27. *Ibid.*

28. *J. Physiol., 17,* 255. In using the technique of cutting motor roots and following their degenerations Sherrington acknowledged that he was following the lead of Carl Sachs (1853–1878). In 1874 Sachs had cut the motor roots of a frog's sciatic nerve and found that a few nerve fibers in the sartorius muscle did not degenerate. The healthy fibers, however, did undergo a slow degeneration when the posterior roots were severed, and this fact led Sachs to conclude that they were sensory fibers.

29. *J. Physiol., 17,* 256.

30. Sherrington, "Note on the knee-jerk and the correlation of action of antagonistic muscles," *Proc. Roy. Soc., 53* (1893), 407–420.

31. Sherrington, "Experiments in examination of the peripheral distribution of the fibres of the posterior roots of some spinal nerves (I)," *Philos. Trans., 184B* (1894), 641. Sir John Rose Bradford (1863–1935), a clinician, teacher, and researcher, was Sherrington's successor as Superintendent of the Brown Institution.

32. For details of these previous studies, see Sherrington's own summaries in his 1894 and 1898 papers: *Philos. Trans., 184B,* 641–648, and "Experiments in examination of the peripheral distribution of the fibres of the posterior roots of some spinal nerves (II)," *Philos. Trans., 190B* (1898), 50–51. Preliminary abstracts of the two papers were published in 1892 and 1897 respectively. The 1898 paper was received by the Royal Society in November 1896 and read in January 1897.

33. The breadth and depth of these studies are illustrated by the five-page table of contents to the 1898 paper, reproduced in Appendix D.

34. *Philos. Trans., 184B,* p. 687.

35. *Philos. Trans., 190B,* pp. 49–50.

36. *Ibid.,* p. 117. Sherrington's thesis about the vertebrate's limb architecture has been borne out by the views of modern comparative anatomists. Alfred S. Romer has observed that "from the first there were notable differences between the front and hind legs of land vertebrates, despite the basic similarity of their bony patterns, and many of these differences are retained in later tetrapods" (*The Vertebrate Body,* 2d ed. [Philadelphia: W. B. Saunders Co., 1955], p. 209).

37. *Philos. Trans., 190B,* p. 152.

38. *Ibid.,* p. 153. An abstract of the Croonian Lecture appeared in 1897 (*Proc. Roy. Soc., 61,* 220–221) before its publication *in extenso* as Part IV of "Experiments in examination . . ."

CHAPTER IV. REFLEX FUNCTIONS: PROBLEMS AND METHODS

1. Sherrington, *The Integrative Action of the Nervous System,* p. 8.

2. Harry D. Patton, "Spinal reflexes and synaptic transmission," in *Neurophysiology,* by T. C. Ruch et al. (Philadelphia: W. B. Saunders Co., 1963), p. 152.

3. John F. Fulton, *Muscular Contraction and Reflex Control of Movement* (Baltimore: The William Wilkins Co., 1926), p. 445.

4. "On the nerves of the orbit," *Philos. Trans., 113* (1823), 289. Sherrington appears to have been both excited and impressed when he discovered Bell's statement, and quoted it as a "remarkable passage" in an addendum to his second note on reciprocal innervation ("Further experimental note on the correlation of action of antagonistic muscles," *Proc. Roy. Soc., 53* [1893], 407–420).

5. For an excellent review of these and other studies of muscle antagonism, see F. Tilney and F. H. Pike, "Muscular coordination experimentally studied in its relation to the cerebellum," *Arch. Neurol. and Psychiat., 13* (1925), 289–334.

6. "Experiments in examination of the peripheral distribution of the fibres of the posterior roots of some spinal nerves (II)," *Philos. Trans. 190B* (1898), 178. Anticipating later discussion, we may note that Sherrington's analysis of reciprocal innervation clarified the nature of antagonistic muscle action primarily at the *spinal* level. In a normal, intact animal, with the "higher centers" operative, antagonistic muscles may be simultaneously contracted during voluntary movements — as Beaunis and Demeny showed. But even in this case the contractions occur in a reciprocal relation: i.e., if an extensor is contracted to 9/10 of its maximum, the opposing flexor may contract to only 1/10 of its maximum, thus maintaining steadiness of movement without antagonism (Fulton, *Muscular Contraction,* pp. 447–448).

7. In modern terms, central inhibition is effected by inhibition within the cord of the motorneurones exciting a muscle, e.g., a skeletal muscle. In peripheral or neuro-effector inhibition, the inhibition is effected by autonomic postganglionic fibers.

8. Brazier, "The historical development of neurophysiology," in *Handbook of Physiology,* p. 36; Charles Mercier, "Inhibition," *Brain, 11* (1888–89), 361–386.

9. "Reflex inhibition as a factor in the co-ordination of movements and postures," *Quart. J. Exptl. Physiol., 6* (1913), 251–310; "The spinal cord," in *Text Book of Physiology,* ed. E. A. Schäfer (Edinburgh: Y. J. Pentland, 1900), p. 838.

10. *Physiologische Studien ueber die Hemmungsmechanismen für die Reflexthätigkeit des Rückenmarks im Gehirne des Frosches* (Berlin, 1863).

11. For a good contemporary review of attacks on and defenses of Setchenov's theory, see W. T. Sedgwick, "Influences of quinine upon the reflex excitability of the spinal cord," *J. Physiol., 3* (1880–1882), 22–36; Alexander Herzen, *Expériences sur les centres modérateurs de l'action réflexe* (Turin, 1864).

12. For more detailed discussions of late nineteenth- and early twentieth-century theories of inhibition, see R. Dodge, "Theories of inhibition," *Psychol. Rev., 33* (1926), 106–122, 167–187; Fulton, *Muscular Contraction,* chaps. xiii–xiv; Fearing, *Reflex Action,* chap. xii. Relevant works by the investigators mentioned in the discussion are cited in the bibliography.

13. Friedrich Goltz, *Beiträge zur Lehre von den Functionen der Nervencentren des Frosches* (Berlin, 1869).

14. *The Integrative Action,* p. 196.

15. Sherrington once told Ragnar Granit that Hering's idea of two fundamentally opposite processes, anabolism and catabolism, held a strong sway among his contemporaries in his early days at Caius. Sherrington also indicated, Granit stated, that Hering's idea strongly influenced his own thoughts and experiments, in addition to stimulating an interest in the physiology of vision (Ragnar Granit, "Sir Charles Sherrington: An Appreciation," *Nature, 169* [1952], 688).

16. W. H. Gaskell, "On the structure, distribution, and functions of the nerves which innervate the visceral and vascular systems," *J. Physiol., 7* (1886), 1–80.

17. For excellent reviews of metabolism theory studies, see A. V. Waller, "On the inhibition of voluntarily and of electrically excited muscular contractions," *Brain, 15* (1892), 35–65, and A. Forbes, "Reflex inhibition of skeletal muscle," *Quart. J. Exptl. Physiol., 5* (1912), 149.

18. McDougall, "The nature of inhibitory processes within the nervous system," *Brain, 26* (1903), 153–191. In relating his theory to spinal cord functions, McDougall drew heavily on Sherrington's reciprocal innervation studies.

19. In a 1925 paper Sherrington incorporated the chemical transmitter theory into his theory of central excitatory and inhibitory states ("Remarks on some aspects of reflex inhibition," *Proc. Roy. Soc., 97B,* 519–545).

20. J. S. MacDonald, "The structure and function of nerve fibres," *Proc. Roy. Soc., 76B* (1905), 322–350. Workers posited a linkage between inorganic salts and inhibition on the basis of observing, for example, the similarity between cardiac inhibition caused by vagal stimulation and that caused by perfusates containing an excess of sodium. *The Integrative Action,* pp. 199, 200.

21. *Ibid.,* p. 1.

22. The persistence of opposition to the neurone theory is indicated by Sherrington's need to defend it at a 1902 discussion on pathology of nerve degeneration. A certain Dr. Stewart had stated, "it is obvious that if, as we have shown, regeneration can occur in the distal segment of a non-united nerve, the so-called 'neuron' theory of Waldeyer can no longer be maintained." Sherrington, in rebuttal, showed why quoting such degenerations is not a valid argument against the neurone theory (*Brit. Med. J., 2* (1902), 928). E. A. Schäfer, *Brain, 16* (1893), 134–169. The

rapidity with which Waldeyer, on the basis of his 1891 conspectus of Cajal's work, was credited as the "founder" of the neurone theory is suggested by the fact that Schäfer cited his article while Cajal's work went unmentioned.

23. A thorough treatment of these topics would entail discussion of the complex history of nerve and neuro-muscular transmission theories. For good brief treatments of transmission studies, see Brazier, "Historical development of neurophysiology," pp. 11–25, and H. Grundfest, "Excitation at synapses," *J. Neurophysiol., 20* (1957), 316–324.

24. Hans Held, "Beiträge zur Struktur der Nervenzellen und ihren Forsatze," *Arch. Anat. und Physiol., Lpz.* (1897), 204; Suppl. (1897), p. 273.

25. *Textbook,* III, 929. Today the synapse is structurally defined as consisting of the synaptic knob, and the synaptic cleft (about 200 Å across) between the knob and the membrane (J. C. Eccles, "The development of ideas on the synapse," in *The Historical Development of Physiological Thought,* ed. Chandler M. Brooks and Paul Cranefield [New York: Hafner, 1959], p. 39). Eccles points out the fact that Sherrington always used "synapse" in its functional sense, restricting it to those areas of close contact that were specialized for effective transmission from one neurone to another (*ibid.,* p. 43).

26. Fulton papers. Arthur W. Verrall (1851–1912), a classical scholar, was a lecturer at Trinity from 1877 to 1911 and became the college's first King Edward VII Professor of English Literature in 1911.

27. Ragnar Granit, *Charles Scott Sherrington: An Appraisal,* p. 43.

28. Leopold Auerbach, "Nervendigung in den Centralorganen," and "Nachtrag zu dem Aufsatz," *Neurol. Zbl., 17* (1898), 445 and 734.

29. In 1903 Cajal began developing a new staining method that would produce the details of the chrome silver stain but also be transparent, revealing the inner structure of the neurone. His reduced silver nitrate formula, as Cannon aptly stated, "was the fulfillment of a histologist's dream": it was a quick and simple stain to apply, could be used widely, produced transparent coloration, and had "exquisite selectivity" for the neurone (Dorothy F. Cannon, *Explorer of the Human Brain: The Life of Santiago Ramón y Cajal,* p. 207).

30. Schäfer, *Brain, 16,* 164; Sherrington, in *Text Book of Physiology,* ed. E. A. Schäfer, p. 608.

31. Sherrington, *Text Book of Physiology,* p. 798. A functional implication of the reticular theory was that the anastomosing nerve network was diffusely conductive in various directions, or perhaps simply trophic for the cells imbedded in it. Cajal's studies of the retina, cerebellum, and spinal cord (1889–1890) convinced him that conduction in the gray matter is perfectly determinate. In every nerve cell, he held, the dendrite and cell body is a receiving apparatus, the axon a transmitting apparatus, and the axon's terminal branches a distributing apparatus that somehow transmits the nerve impulse to the dendrites of a contiguous neurone. To Cajal this determinate, unchanging direction of nerve conduction implied a sort of permanent orientation, analogous to the attraction of the magnetic pole. Thus, he termed his theory of nerve conduction "ley del la polarizacion

dinamica de la celula nervosa" — "the law of dynamic polarization" (Ramón y Cajal, *Recollections of My Life,* chap. viii).

32. *The Integrative Action,* p. 17.

33. One element in Sherrington's success as an experimenter, his son commented, was that "he was first rate with his hands, whether operating or metal working. Until 75 he had a wonderfully steady hand, and could sign-write like an engraver impeccably" (Carr Sherrington, Personal communication, December 28, 1964).

34. April 2, 1930. In his notes for the same day Fulton wrote: "[Sherrington] emphasized several times today that the only people who really understand the nervous system were those who made their own preparations." Sherrington wryly remarked on an extreme instance of "personal investigation" in a letter to Fulton of December 10, 1925: "I have been going through a little first-hand experience in muscle-physiology — on my biceps. A torn biceps soon informs one that muscle possesses 'pain'-afferents among other centripetals; also that their reflex effect is invincible inhibition of voluntary use of the muscle. However, here I am *writing* again quite comfortably . . ." (Fulton papers).

35. "Foreword to the 1947 edition," *The Integrative Action,* p. xii.

36. A modern textbook describes decerebrate rigidity as a state of hyperactivity of the stretch reflexes caused by sectioning the brain stem at midbrain level, leaving the pons and medulla intact and connected with the cord through their descending vestibulo- and reticulospinal tracts. With transection there is a marked and prompt decrease in the excitability of the stretch and other extensor reflexes and an increase in the excitability of the flexor reflex (T. C. Ruch, *Neurophysiology,* pp. 202, 206).

37. "Decerebrate rigidity, and reflex co-ordination of movements," *J. Physiol., 22* (1898), 319–332. In view of Sherrington's extensive historical knowledge, it is surprising that he stated in the 1898 paper that he had found no descriptions of decerebrate rigidity prior to that given in his third note on reciprocal innervation (*Proc. Roy. Soc., 60* [1897], 414–417. As he later discovered, the decerebrate posture, known clinically as "opisthotonus," had long been recognized by clinicians: Giorlamo Cardano described an opisthotonic child in his 1575 autobiography (F. F. Jones, "A Note on the Latinity of Sir Charles Sherrington," *American Scientist, 51* (1963), 403–407). François Magendie, a researcher well known to Sherrington, had clearly described the decerebrate posture in a rabbit in 1823 (J. M. D. Olmsted, *François Magendie,* p. 126).

38. Pierre Flourens, *Recherches Expérimentales sur les Propriétés et les Fonctions du System Nerveux dans les Animaux Vertébrés* (Paris, 1824). Flourens' description of the decerebrate pigeon did not mention the muscle spasm of decerebrate rigidity; Sherrington, *J. Physiol., 22,* 319.

39. Vulpian's noted text, *Leçons sur la Physiologie du Système Nerveux,* was a work which Sherrington "had read as a young man and remembered with pleasure all his life" (E. G. T. Liddell, *The Discovery of Reflexes,* p. 90). H. Sanders-Ezn, "Vorarbeit für die Erforschung des Reflex-mechanismus im Lendenmark des Frosches," *Ludwig's Arbeiten Physiol. Anat., 2* (1868), 1.

40. Figure 1, Plate 17, of Sherrington's 1899 Marshall Hall Prize Ad-

dress, showing a decerebrate monkey, is dated Nov. 18, 1894; *Proc. Roy. Soc., 60* (1897), 413. Sherrington termed the reflexes "cataleptoid" because they recalled certain phases of hypnotic catalepsy, and because the strict significance of the prefix implied "a steady maintenance of possession subsequent to seizure." He observed that the "cataleptoid" posture of one forelimb could be inhibited by stimulating the other forelimb — one of the first clear demonstrations of a definite cross-inhibitory effect between forelimbs.

41. *Proc. Roy. Soc., 60,* 414–417; *Philos. Trans., 190B,* 159, 161. In the lecture Sherrington carefully distinguished between "decerebrate tonus," "decerebellate tonus," "normal tonus," "spinal tonus," and "late rigidity." Normal muscle tonus, he noted, doubtlessly is the result of an "algebraically summed number of spinal, cerebral, and cerebellar factors." The spinal animal's "spinal tonus" is a remnant of the normal tonus. In some of his monkeys a marked "late rigidity" or "paraplegia" developed in the lower limbs after transection of the cord in the lower thoracic region. He attributed this type of rigidity to an "upset of the balance of the spinal tonus in antagonistic muscle groups," and held that its origin is reflex in nature.

42. The following discussion has been synthesized from four of Sherrington's works on decerebrate rigidity: "Decerebrate rigidity, and reflex co-ordination of movements," *J. Physiol., 22* (1898), 319–332; "Path of impulses for inhibition under decerebrate rigidity," *J. Physiol., 28* (1902), 14–19; "A pseudaffective reflex and its spinal path," *J. Physiol., 31* (1904), 234–243; *The Integrative Action,* pp. 299–305.

43. *J. Physiol., 22,* 323.

44. *The Integrative Action,* p. 301. Sherrington had ruled out the cerebellum as the seat of this cranial mechanism by showing that decerebellation does not abolish the rigidity.

45. J. Hughlings Jackson, "The Croonian Lectures on evolution and dissolution of the nervous system," *Brit. Med. J., 1* (1884), 591–593, 660–663, 703–707. Earlier workers such as Hall and Bell had recognized the fact of release of function when they observed that reflexes below a transection become stronger or more easily elicited.

46. Sherrington began to develop his thesis in *The Integrative Action,* and explored it more fully in "Postural activity of muscle and nerve," *Brain, 38* (1915), 191–234. Henry Head, "Release of function in the nervous system," *Proc. Roy. Soc., 92B* (1921), 184–208.

CHAPTER V. RECIPROCAL INNERVATION (1893–1900)

1. Sherrington, "Reflex inhibition as a factor in the co-ordination of movements and postures," *Quart. J. Exptl. Physiol., 6* (1913), 307–308.

2. "The analysis of the nervous system. Sherrington Memorial Lecture," *Proc. Roy. Soc. Med., 50* (1957), 993.

3. In this and the following chapter I will deal only with "Notes" 1–9 (1893–1906). The sequence of study in the "Notes" may be summarized briefly as follows: 1 (1893), antagonistic relation between extensors and flexors in the knee jerk; 2 (1893), correlation of action in eye muscles and

eyelid apparatus; 3 (1897), correlation of action between flexors and extensors in hind limb; 4 (1897), reciprocal innervation in limb muscle groups evoked by cortical stimulation; 5 (1898), reciprocal innervation in eyelid apparatus; 6 (1900), reciprocal innervation in hind limb reflexes of frog deprived of cutaneous receptors; 7 (1905), successive spinal induction; 8 (1905), interrelations between muscles involved in moving the knee joint; 9 (1906), successive spinal induction; 10 (1907), general observations on reciprocal innervation in hind limb muscles; 11 (1907) successive induction; 12 (1908), lengthening and shortening reactions characterizing the extensors in decerebrate rigidity; 13 (1908), algebraic summation of inhibitory and excitatory stimuli converging simultaneously on a motor center; 14 (1909), double reciprocal innervation.

4. "Note on the knee-jerk and the correlation of action of antagonistic muscles," *Proc. Roy. Soc., 52* (1893), 563.

5. Francis Gotch, "Note on the so-called tendon reflex," *J. Physiol., 20* (1896), 322–333.

6. As Ragnar Granit has observed, "it is hard to realize the great difficulty at the beginning of establishing that inhibition is an *active* process, and not mere absence of activity" (*Charles Scott Sherrington: An Appraisal,* p. 51).

7. *Proc. Roy. Soc., 52,* 563. As noted in Chap. III, it was this finding which led Sherrington to his study of sensory nerves in muscles.

8. Hering and Breuer first showed the role of the afferent fibers of the vagus nerve in controlling respiration. As Sherrington's experiments subsequently established, peripheral inhibition does not occur in mammalian muscles; their motor control is effected by central inhibition alone. His initial belief that central and peripheral inhibition are "not widely different," however, is now recognized as sound. For, as Granit has stated, "it has taken us half a century of experimentation to come back to Sherrington's original models and realize that fundamentally both central and peripheral inhibitions are run on the same pattern" (*Charles Scott Sherrington: An Appraisal,* p. 56).

9. Sherrington reported further work on the palpebral apparatus in his fifth "Note" (*Proc. Roy. Soc., 64* [1889], 179–181).

10. This doctrine, as was noted in Chap. IV, was further supported by Sherrington's study of the causes of decerebrate rigidity.

11. "Further experimental note on the correlation of action of antagonistic muscles," *Proc. Roy. Soc., 53* (1893), 414–415. In an addendum to this paper Sherrington reported that the inhibition of active contraction caused either volitionally or by cortical stimulation is not confined to the external rectus but occurs also in other ocular muscles, such as the internal rectus. His additional experiments on the internal rectus apparently were stimulated by his discovery of Charles Bell's "remarkable passage" (see above, p. 69).

12. "On reciprocal innervation of antagonistic muscles. Third note," *Proc. Roy. Soc., 60* (1897), 414–417; "Experiments in examination of the peripheral distribution of the fibres of the posterior roots of some spinal nerves. (II)," *Philos. Trans., 190B* (1897), 178.

13. Sherrington later recognized that reciprocal innervation plays a

minor role at best in "willed" and "high level" reflex acts. "Many observations," he wrote Fulton on May 12, 1926, "indicate that if it does so it is overlaid by other complicated factors — and is not simple and evident in them. A case in which it seems to dominate in high level movement is that of conjug-lat. deviation of the eyeballs executed from the cortex in the monkey; but even there directly convergence is at work . . ." (Fulton papers).

14. "On reciprocal innervation of antagonistic muscles. Third note," *Proc. Roy. Soc., 60* (1897), 416. This point is one which Sherrington stressed repeatedly in later years: the principle of reciprocal innervation is strictly applicable only in the isolated cord. For, with the brain operative, its higher levels of nerve control may "override" the spinal reflex apparatus to provide co-contraction of antagonists. In papers of 1897 and 1899 Sherrington and H. E. Hering reported on reciprocal innervation in voluntary muscles produced by excitation of the cerebral cortex ("Antagonistic muscles and reciprocal innervation. Fourth note," *Proc. Roy. Soc., 62,* 183–187; "Inhibition of the contraction of voluntary muscles by electrical excitation of the cortex cerebri," *J. Physiol., 23,* 31).

15. "Inhibition of the tonus of a voluntary muscle by excitation of its antagonist," *J. Physiol., 23,* 26.

16. "On the innervation of antagonistic muscles. Sixth note," *Proc. Roy. Soc., 66,* 66–77.

17. "Decerebrate rigidity and reflex co-ordination of movements," *J. Physiol., 22,* 332.

18. *Philos. Trans., 190B,* 180.

19. "On the spinal animal," *Med.-Chir. Trans., 82* (1899), 462.

20. "The spinal cord," in Schäfer's *Text Book,* p. 784; *Med.-Chir. Trans., 82,* 451. The "way in" and the "way out" of the afferent and efferent root-cells are analyzed in detail by Sherrington in Schäfer's *Text Book,* pp. 787–811.

21. Sherrington often referred to the distance receptors as the "great projicient organs": i.e., they are the same receptors which, acting as sense organs, initiate sensations with the "psychical" quality of "projection" or "projicience" (*The Integrative Action of the Nervous System,* p. 324).

22. Schäfer's *Text Book* contains a full chapter by Sherrington on the muscular sense, in which he discusses its role in posture, passive and active movements, and its fusion with other senses to provide spatial qualities. The fact that a full chapter could be devoted to this subject in 1900 was due, in no small measure, to his own researches.

23. *Med.-Chir. Trans., 82,* 464, 465.

24. *Philos. Trans., 190B,* 145. "Block delimitation" refers to an arbitrary fraction of the spinal cord included between two imaginary frontal segments, placed one on each side of a nerve pair, and each halfway between the next nerve pair below and the next above.

25. *Med.-Chir. Trans., 82,* 465.

26. The Pflüger-Lotze debate raged around two issues. First, does the behavior of the spinal animal show the existence of *consciousness?* This question involves the metaphysical issue of whether the "soul" or "consciousness" is divisible, and the physiological point of whether any move-

ments of the spinal animal are independent acts of volition. Second, do the spinal animal's coordinated movements show the existence of *intelligent* purposiveness? (Franklin Fearing, *Reflex Action: A Study in the History of Physiological Psychology,* chap. xi.)

27. *Med.-Chir. Trans., 82,* 469. Sherrington devoted his seventh Silliman Lecture to an analysis of reflex purposiveness in terms of Darwinian theory. It is, he stated, equally impossible to prove or disprove the notion that "psychical events" accompany the nervous reactions of a spinal animal. But, he felt, the whole question largely has been made superfluous by Darwinian theory, for that theory "suggests how purposive neural mechanisms may arise. It furnishes a key to the genesis and development of adapted reactions, and, among these latter, reflexes" (*The Integrative Action,* p. 236).

28. *Med.-Chir. Trans., 82,* 469; "The spinal cord," in Schäfer's *Text Book,* p. 858.

29. *Philos. Trans., 190B,* 133. Sherrington here echoes Foster's caution to students (see above, p. 45).

30. The analysis of Sherrington's "rules" is drawn from his statements in "The spinal cord," in Schäfer's *Text Book,* pp. 819–845, and the Croonian Lecture (*Philos. Trans., 190B,* 145–177). In the latter Sherrington described the "fundamental experiments" demonstrating each rule and noted any apparent exceptions to it.

31. "The spinal cord," in Schäfer's *Text Book,* p. 823. The laws, in brief, stated Pflüger's views on (1) homonymous contraction for unilateral reflexes, (2) bilateral symmetry of reflex action, (3) unequal intensity of bilateral reflexes, and (4) direction of spread (toward the head) of irradiation with associated spinal reflexes.

32. "The spinal cord," in Schäfer's *Text Book,* p. 824.

33. *Ibid.,* p. 819. Unless otherwise noted my discussion of the five rules is drawn and quoted from *Philos. Trans., 190B,* 145–168.

34. Sherrington determined the primary spinal reflexes in order of ease of production for the upper and lower limbs of Macacus (*Philos. Trans., 190B,* 155).

35. "The spinal cord," in Schäfer's *Text Book,* p. 820.

36. *Ibid.,* p. 821.

37. *Philos. Trans., 190B,* 162.

38. Hall, *Synopsis of the Diastaltic Nervous System* (London: 1850), p. 70. Foster, we have noted, cautioned students to be aware of the effects of shock when studying spinal reflexes. Similarly, Sherrington warned that "it is the ill-understood phenomenon known as 'shock' that especially tends to obscure the segmental analysis of the spinal functions in higher animals" ("The spinal cord," in Schäfer's *Text Book,* p. 816).

39. Sherrington, *Philos. Trans., 190B,* 134; Friederich Goltz, "Ueber die Functionen des Lendenmarkes des Hundes," *Pflüg. Arch. ges. Physiol., 8* (1873–74), 460–486.

40. Sherrington, "A note on the physiology of the spinal cord," *St. Thomas's Hospital Reports, 23* (1896), 69–76.

41. *Philos. Trans., 190B,* 142.

42. *Ibid.,* pp. 136, 139. Sherrington observed two monkeys for six and

five months respectively without noting any improvement in their reflexes.

43. *Ibid.,* pp. 141–142.

44. *Ibid.,* pp. 143–144.

45. *Med.-Chir. Trans., 82,* 475. In the Silliman Lectures Sherrington summarized and strengthened his view of "shock" in higher forms as a "true deficiency phenomenon." He maintained, in brief, that: (1) shock is not due to traumatic irritation, for it occurs when the cord is functionally sectioned atraumatically by cooling or a procaine injection; (2) the condition of the spinal reflex arcs in shock appears to resemble general spinal fatigue rather than "inhibition"; (3) shock appears to be induced by the "rupture of certain aborally conducting paths . . . from some nucleus of the pontine or midbrain system, driven probably by the great cranial receptors . . . reinforced by impulses from the cord itself" (*The Integrative Action,* pp. 241–248).

46. "The spinal cord," in Schäfer's *Text Book,* p. 843.

47. *Ibid.,* p. 844.

48. *Ibid.,* p. 837. Sigmund Exner's term "Bahnung," Sherrington noted, is a "felicitous expression" not easily translated into English. Some of the phenomena covered by "Bahnung" had been designated as "augmentation," "canalization," and "reinforcement," but "facilitation," to Sherrington, "perhaps most nearly expresses what is intended."

49. *Ibid.,* pp. 840–841.

50. *Ibid.,* pp. 841–842.

51. *Ibid.,* p. 842. In a footnote to this passage Sherrington recognized that his scheme of "reciprocal inhibition" differed from the views of inhibition presented by workers such as Goltz, Wundt, Herzen, and Schiff.

52. *Ibid.,* p. 837.

CHAPTER VI. THE SCRATCH REFLEX PARADIGM

1. Sherrington and Laslett, "Note upon descending intrinsic spinal tracts in the mammalian cord," *Proc. Roy. Soc., 71* (1902), 115–121. Their method involved placing two or more successively degenerating lesions at long intervals (9–10 months). The first degeneration acts to remove all fiber tracts other than those to be studied, while the second acts on the tracts in question. Following the second degeneration the tissue is prepared by the Marchi method.

2. "Observations on some spinal reflexes and the inter-connection of spinal segments," *J. Physiol., 29,* 58–96. The four reflexes studied were: (1) scratch, (2) a simultaneous movement in all limbs caused by stimulating the skin mid-dorsally near the shoulder, (3) "shake" — alternating movements of rump and tail elicited by rubbing the skin of the mid-dorsum, loin, or sacrum, and (4) "hand-foot" — movements in the hind limb caused by stimulating the forepaw. Nine short reflexes also were studied, chiefly as controls.

3. Haycraft, "Reflex spinal scratching movements in some vertebrates," *Brain, 12* (1889), 516–519.

4. Although the spinal dog's scratch reflex is vigorous, his paw never

actually reaches the point irritated. Thus, as Sherrington later observed, the reflex "fails to effect the object for which it seems obviously adapted" ("Observations on the scratch reflex in the spinal dog," *J. Physiol., 34* (1906), 45).

5. It is now thought that the spinal dog's scratch reflex is more likely to be polysynaptic than disynaptic.

6. Sherrington, "Qualitative difference of spinal reflex corresponding with qualitative difference of cutaneous stimulus," *J. Physiol., 30* (1903), 39–46. He had reported earlier studies of the direct extension reflex in his sixth "Note" (*Proc. Roy. Soc., 66* [1900], 66–67).

7. *J. Physiol., 31,* xvii–xix.

8. "The correlation of reflexes and the principle of the common path," *Brit. Assoc. Rep., 74* (1904), 2. Sherrington also began his first Silliman Lecture by delineating these three lines of investigation.

9. *Brit. Assoc. Rep., 74,* 2.

10. *Ibid.*

11. *Ibid.,* p. 3.

12. *Ibid.*

13. *Ibid.,* p. 4.

14. Mutual reinforcement, he found, cannot be demonstrated for all the arcs arising in the receptive field of the scratch reflex: there seems to be a gradual fall in reinforcing power as the distance between the receptors increases.

15. *Brit. Assoc. Rep., 74,* 8. Sherrington here has described a case of "immediate spinal induction" (see below, pp. 115–116).

16. *Ibid.,* p. 6.

17. *Brit. Assoc. Rep., 74,* 7.

18. *Ibid.,* pp. 12, 13.

19. *Ibid.,* p. 14.

20. *Ibid.,* pp. 12,10.

21. "On reciprocal innervation of antagonistic muscles. Seventh note," *Proc. Roy. Soc., 76B* (1905), 160–163; "On the innervation of antagonistic muscles. Ninth note. Successive spinal induction," *Proc. Roy. Soc., 77B* (1906), 478–497. When a spinal dog is supported so that its spine is vertical and its hind limbs hang freely the limbs begin to perform a rhythmic stepping movement — the *mark-time reflex* first described by Goltz and Freusberg in 1874. The stepping movements, Sherrington noted, may last up to twenty minutes and are effected chiefly by flexion at hip and knee.

22. *Proc. Roy. Soc., 77B,* 483. The resemblance between reflex rebound and visual induction had been pointed out earlier by both Sherrington (*J. Physiol. 21* [1897], 33–54) and William McDougall (*Brain, 26* [1903], 153–191).

23. *The Integrative Action,* p. 121; *J. Physiol., 34,* 27.

24. Loeb, *Vergleichende Gehirnphysiologie* (*Leipzig,* 1899), p. 96; Uexküll, "Studien über Tonus. I. Der biologische Bauplan von Sipunculus nudus," *Ztschr. f. Biol., 44* (1902–03), 269–344.

25. *Proc. Roy. Soc., 76B,* 162.

26. "On reciprocal innervation of antagonistic muscles. Eighth note," *Proc. Roy. Soc., 76B* (1905), 269. Sherrington realized that to make a valid

comparison between inhibition and excitation one needs to study both processes in the same *type-reflex,* for even in one spinal region the modes of origin, time-relations, etc., of different type-reflexes will differ greatly. A *type-reflex* is a reflex such as direct extension or scratching which, though given a general name, actually is composed of a number of more or less similar reflexes.

27. *Ibid.,* p. 276. The correspondences which Sherrington observed included: (1) excitation and inhibition of the reflex (as seen in the two limbs) were elicited from the same skin-field; (2) stimulation of a given nerve-twig in the "flexor limb" excited the flexors; stimulation of the corresponding nerve-twig in the "extensor limb" inhibited the extensors; (3) the responses of each limb were similar in features such as latent time, gradation, summation, and aftereffect.

28. *Ibid.,* p. 283. See above, p. 102 (Sherrington's 1900 schemata of "reciprocal inhibition").

29. Sherrington noted that after-discharge, with its concomitant persistence of contraction, might be disadvantageous to the organism. Therefore, he commented, its rapid arrest by the inhibitory side of a succeeding reflex is an adaptation which facilitates the successive interchange of reflexes (*Proc. Roy. Soc., 76B* [1905], 285).

30. In view of the active nature of inhibition and its known ability to excite opposed muscles synchronously in certain voluntary movements, Sherrington ran a number of experiments in which he stimulated different afferent nerve-twigs and skin-points to see if spinal inhibition could be changed into excitation. With the single exception of the plantar surface, from which certain innocuous mechanical stimuli regularly elicited extensor contraction rather than relaxation, his results were negative (*Proc. Roy. Soc., 66* [1900], 66; *J. Physiol., 30* [1903], 39).

31. *Proc. Roy. Soc., 76B,* 287. Sherrington devoted the last ten pages of the eighth "Note" to explaining the abnormal changes in the central condition of the cord induced by strychnine or tetanus toxin in terms of this hypothesis. "The action of the alkaloid in the spinal cord," he suggested, "is to convert the process of inhibition — whatever that may essentially be — into the process of excitation — whatever that may essentially be. The nexus was pre-existent, but the effect across it was signalized by a different sign — *minus* prior to the strychnine or tetanus toxin, instead of *plus,* as afterward." This explanation and the hypothesis behind it, he felt, accounted for the simultaneous contraction of large groups of inharmonious muscles seen in strychnine convulsions: the poison has destroyed the spinal taxis for skeletal muscles by upsetting the fundamental coordination of reciprocal innervation.

32. "On the proprio-ceptive system, especially in its reflex aspects," *Brain, 29* (1906), 467–482.

33. *Ibid.,* p. 472.

34. *Ibid.,* p. 473. Reinforcement of a primary reflex is illustrated by a subliminal stimulus of the skin of the foot (surface receptor) becoming effective when stimulation of an afferent nerve of the flexor muscle (proprioceptor) is delivered synchronously. A compensatory reflex, for example, is evoked when an afferent nerve of the left limb's flexors is stimulated,

causing reflex inhibition to cut short the flexion reflex provoked from the skin of the right leg.

35. *Brain, 29,* 473, 474.

36. *Ibid.,* p. 474. Sherrington's view that tone is a postural reflex was generally accepted during his lifetime. "Today," Ragnar Granit observes, "while one would still be willing to give the postural reflex a role to play in tone, it seems impossible to identify the two concepts" (*Charles Scott Sherrington: An Appraisal,* p. 155).

37. *Brain, 29,* 475.

38. *Ibid.,* pp. 482, 478–480, 476.

39. "Observations on the scratch-reflex in the spinal dog," *J. Physiol., 34* (1906), 1–50.

40. *Ibid.,* p. 42.

41. *The Discovery of Reflexes,* p. 136. To Ragnar Granit, from the viewpoint of a neurophysiological researcher, Sherrington's studies of the ipsilateral flexor, crossed extensor, and stretch reflex "proved to be of greatest importance" for the development of knowledge about reflex excitation, inhibition, antagonism, and interaction. Sherrington himself, Granit acknowledges, "may well have been more interested in the scratch reflex . . . But any appraisal of Sherrington from perspectives valid today must throw the emphasis differently and start with [the flexor, extensor, and stretch reflexes] . . . they became instrumental in advancing the theory while the scratch reflex . . . as such the work of an experimental perfectionist and complete in itself, has remained a beautiful thing on the shelf, too complex for the terms in which we think, struggling as we are with the development of first principles" (*Charles Scott Sherrington: An Appraisal,* p. 62). While Granit's appraisal is sound from the viewpoint of a neurophysiologist today, *historically* the scratch reflex was of major importance in Sherrington's development of the integrative action concept.

CHAPTER VII. REFLEXES AND MOTOR INTEGRATION

1. The Lectureship had been established in 1901 with a legacy of $80,000 left to Yale College in 1883 by Mr. August Ely Silliman in memory of his mother. According to the terms of the bequest the Silliman Lectures were to be an annual series on a topic of natural science or history; they were to be published and should illustrate in their content "the presence and wisdom of God as manifested in the Natural and Moral World." In 1903 J. J. Thomson of Cambridge University inaugurated the Lectures, speaking on "electricity and matter" (*Yale Historical Register,* "Silliman Memorial Lectureship"; W. Osler, *The Evolution of Modern Medicine,* 10th Silliman Lectures [New Haven: Yale University Press, 1921], Preface).

2. February 24, 1904 (Fulton papers). There is little information available on the circumstances of Sherrington's invitation to Yale. In a letter to John Fulton of February 6, 1935, Charles H. Warren of Yale's Sheffield Scientific School wrote: "I find upon investigation that I have no correspondence in my files relating to the Silliman Lectures of the first few years. Where it has gone, I have no idea" (Fulton papers).

3. Letter from Chittenden to John Fulton, March 16, 1935 (Fulton papers).

4. [Notice of Sherrington's visit to Yale], *Yale Alumni Weekly,* May 18, 1904, p. 716.

5. See Appendix E for the syllabus of the lectures; letter to Fulton, March 16, 1935. "According to John Fulton," Ragnar Granit states, "the large audience had dwindled to four people at the last lecture" (*Charles Scott Sherrington: An Appraisal,* p. 48).

6. *Sherrington: Physiologist, Philosopher, Poet,* p. 14. Sherrington apparently found his lectures as trying as did his audiences. As one of his students recalled, it was notorious among those who worked with him that he should not be approached in the hour or more preceding and the half hour following a lecture (Creed, *Brit. J. Psychol., 44,* 4).

7. "Silliman Lectures. Review of the course given at Yale by Professor Sherrington," *Yale Alumni Weekly, 13* (May 18, 1904), 715–716. In a letter to John Fulton dated March 21, 1935, Henderson expressed his feelings about Sherrington's lecture style far more frankly: "I hesitate to put down on paper my recollections of the impression that [his] unfortunate mode of delivery made upon his general audience . . . My general feeling is . . . that it is best forgotten" (Fulton papers).

8. "Review of *The Integrative Action of the Nervous System,* by Sir Charles Sherrington," *Brit. Med. J., 1* (1907), 567.

9. Personal communication, November 23, 1964. Professor Liddell, one of Sherrington's Oxford colleagues, also recalled that "recruitment," "eclipse," and "occlusion" were words which Sherrington introduced only after several weeks of contemplation.

10. Fulton papers.

11. "A foundation of neurology. *The Integrative Action of the Nervous System.* By Sir Charles Sherrington," *Brit. Med. J., 2* (1947), 823.

12. I had hoped to collate the original Silliman Lectures and *The Integrative Action,* but neither the Yale Press or Mr. Carr Sherrington know what became of the manuscripts of the Lectures and book (Personal communication from Jane Olson, editor, Yale Press, March 19, 1965; Personal communication from Carr Sherrington, May 10, 1965).

13. Lecture X falls on the whole outside the scope of this study, but it does illuminate Sherrington's stand on the mind-body problem and his views on psychology. I have included a brief analysis of this material in Appendix F.

14. Unless otherwise noted, the "Silliman Lectures" henceforth refers to their published form, *The Integrative Action.*

15. Throughout this chapter, page numbers for quotations from *The Integrative Action* are given after the quotation.

16. The major physiological concept of the *milieu interieur* was developed by the French physiologist Claude Bernard (1813–1878). Bernard held, in brief, that the blood forms a controlled and constant fluid medium, the *internal environment,* which mediates between the life of the organism and its external environment.

17. Sherrington noted that solid intercellular material provides integration by the "mechanical" combination of individual cells into various

masses, while fluid intercellular material such as blood and lymph provides a field for chemical integration.

18. Sherrington reserved discussion of fatigue, facilitation, and shock (items 7, 9b, 9d) for later lectures.

19. Since the neurone theory was still a controversial topic in 1904–1906, Sherrington perhaps judiciously tempered his acceptance of it with statements such as: "it seems therefore likely that the nexus between neurone and neurone in the reflex-arc, at least in the spinal arc of vertebrates, involves a surface of separation" (*The Integrative Action,* p. 17). Before stating that synapses are responsible for the properties of reflex arc conduction, he ruled out four histological constituents found in the gray matter: perikarya (nerve cell bodies), dendrites, axons, and neuroglia (neural connective tissue).

20. As we have noted, the nature of nerve and neuromuscular transmission was largely conjectural when Sherrington was writing. On pp. 16–17 of *The Integrative Action* he briefly suggested how the synapse could operate if the neurone's conductive element is either a "fluid" (chemical) or an "electric" (physical) process.

21. By the turn of the century it was known that the latent period for a nerve trunk response is entirely a propagation time, proportional to the distance between the seats of stimulus and response, while reflex latency is inversely proportional to stimulus intensity. Sherrington felt that this intensity effect is more significant than the "mere" greater slowness of reflex versus nerve trunk conduction, or the fact that reflex conduction times vary among different type-reflexes. On the basis of his studies of reflex time in initial and incremental flexion reflexes, he argued that reflex latency is "inherent in the process of [synaptic] transmission" (*The Integrative Action,* p. 25). Sherrington's study of reflex scratching had impressed upon him the uniqueness of a reflex's after-discharge.

22. Refractory phase was first recognized in 1874 by Krönecker and Stirling in the cardiac rhythm. As named and defined by Marey in 1876, refractory phase meant the time during which the heart was inexcitable to a stimulus of any intensity. The first reflex arc refractory phase was recognized in 1899 by Zwaardemaker and Lans, when they were studying reflex eyelid closure. By 1904, with the recognition of absolute and relative refractoriness, "refractory phase" meant "a state during which, apart from fatigue, the mechanism shows less than its full excitability" (*The Integrative Action,* p. 45). Sherrington devoted ten pages of Lecture II to summarizing the architecture of the scratch reflex in the spinal dog as a basis for his analysis of the refractory phase (*ibid.,* pp. 45–56).

23. A "Medusa" is the sexual phase in the life cycle of coelenterates (hydra, jelly fishes, etc.), the first true multicellular animals to have their body cells organized into definite tissues. Medusa's locomotion is effected through its unpolarized nerve-net system, which allows a single stimulus at any point to evoke a full and coordinate beat of its swimming bell.

24. Sherrington noted that many other reflexes, such as swallowing, blinking, and stepping, evidence a prominent central refractory state, and that these reflexes, like scratching, are concerned with cyclic actions occurring in rhythmic series.

25. His discussion, accompanied by many myograms, draws heavily upon his well-documented knowledge of the knee jerk, flexion, and extension reflexes.

26. The content and often the wording of Lectures IV–VI are in large part a skillful blending of many of Sherrington's major papers: his 1897 and 1904 Croonian and British Association addresses, the long 1906 papers on the scratch reflex and on the proprioceptive system, the "Notes," and the papers on sensory and motor pathways.

27. Sherrington adopted the word "complication" from the German philosopher-psychologist J. F. Herbart (1776–1841). In his 1825 *Psychologie als Wissenschaft,* Herbart used "complication" to describe the associative combination of different sensations, such as a sound and a color.

28. With regard to the dog's scratching reflex Sherrington suggested, half facetiously, that "it is perhaps to avoid the consequences of the spatial spread of the 'Bahnung' that the hop of the flea has been developed" (*The Integrative Action,* p. 185).

29. This is not to say, Sherrington cautioned, that the onset of one reflex is uninfluenced by the existence of the other. The second reflex's latent period, for example, is liable to be greatly influenced by the first reflex.

30. An example of the successive combination of antagonistic reflexes is the scratch reflex's displacement by a prepotent flexion reflex. A converse displacement is depicted in Fig. 13.

31. Sherrington's terminology with respect to the process underlying reflex antagonism is confusing. In Lecture IV he first refers to the process as *interference* and says that it is "tantamount to, if not the same thing as, inhibition" (p. 143). In Lecture VI, however, he distinguishes between "interference" and "inhibition" as two forms of active intervention effecting a smooth transition between antagonistic reflexes (pp. 192–206). He adopted the word "interference" from Wundt and Tschermak, who used it with no reference to the physicists' connotation of a mutual interference between vibrations. In Lecture VI Sherrington uses "interference" to designate the transition from one simultaneous double-sign reflex to an antagonistic double-sign reflex (p. 200). In this sense, "interference" embraces both inhibitory and excitatory processes. Sherrington also delineated the phenomenon of *partial interference*: in the case of two complex or type-reflexes, their component reflexes may be allied in regard to one part of their multiple final common path and be antagonistic in regard to another part of it (Lecture IV, pp. 145–146).

32. "Alternating reflexes" had been discussed by Sherrington in his Croonian Lecture and "Notes" on reciprocal innervation. An "active compensatory reflex" is seen when a decerebrate animal's limb returns to its usual posture of extensor rigidity after the induction of a flexion reflex: the two reflexes, extensor and flexor, are diametrical antagonists.

33. *The Integrative Action,* pp. 207–232. Sherrington had enumerated the last three factors in his "Common Path" address (1904). His analysis of spinal induction, as I have noted, was not completed until the ninth "Note" in 1906. The Yale Silliman Lectures' syllabus does not mention "induction," indicating that his views on it were formulated between

1904 and 1906. Sherrington's analysis of the role of fatigue in reflex action and its intraspinal, "probably" synaptic, locus was based on his work with the scratch and flexion reflexes (*The Integrative Action,* pp. 215–224). Fatigue sets in under continuous excitation or frequent repetition of a stimulus: a reflex becomes progressively weaker, declining in amplitude and in steadiness of rhythm, and finally may cease altogether. In Sherrington's colorful words, "fatigue helps to ensure serial variety of reaction. The organism, to be successful in a million-sided environment, must in its reactions be many-sided. Were it not for . . . fatigue, an organism might, in regard to its receptivity, develop an eye, or an ear, or a mouth, or a hand or leg, but it would hardly develop the marvelous congeries of all the various sense organs which it is actually found to possess" (*The Integrative Action,* pp. 223–224).

34. From his study of the scratch reflex Sherrington had identified facilitation, and therefore also spinal induction, as a special form of summation.

35. See above, pp. 92–93.

36. Sherrington illustrated one method of unraveling a reflex's purpose by reviewing his and Woodworth's study of *pseudaffective reflexes*: mimetic movements in a decerebrate cat simulating expression of certain affective states, such as pain. By analyzing the mimetic reflex's components, its effective stimuli, and the neural paths involved, Sherrington and Woodworth gained a picture of how a normal animal may respond to nocuous stimuli ("A pseudaffective reflex and its spinal path," *J. Physiol., 31* [1904], 234–243; *The Integrative Action,* pp. 252–256).

37. Sherrington devoted ten pages of Lecture VII to the topic of spinal shock. His discussion centered around his differences of opinion with Goltz's view of shock as a long-lasting inhibition due to trauma.

38. By "emotion" Sherrington referred to the "coarser" or "animal" emotions such as rage, fear, and anger.

39. Sherrington, *Proc. Roy. Soc., 66* (1900), 390–403. In the early years of the twentieth century three hypotheses stood as possible explanations for the "bodily resonance of emotion": (1) the visceral reaction is secondary to and generated by the psychical part of the emotion; (2) the psychical and visceral reactions are collateral and concurrent; and (3) James's and Lange's view: the psychical process is secondary to the visceral. James's theory of emotion, his most famous and widely discussed psychological theory, was first presented in 1884 ("What is emotion?" in *Mind, 9,* 188–204). He argued, in brief, that the nervous system makes certain innate or reflex adjustments to emotional stimuli, and these adjustments automatically lead to bodily changes, mainly in the viscera and skeletal muscles. Some of these changes can be felt, and their perception *is* the emotion. In 1885 Carl Lange of Copenhagen published a theory similar to James's, although not as extreme, tracing the psychophysiology of emotion to vasomotor changes.

40. Sherrington was fully cognizant of the major obstacle to any excursion into animal psychology: "We are, of course, in observations such as this, hopelessly cut off from introspective help" (*The Integrative Action,* p. 266). He also attempted to answer possible criticisms of his

interpretation of the dogs' "emotions," most notably that "although the animals expressed emotion they may yet have *felt* none"; and he discussed the possible validity of the hypothesis that the psychical and visceral elements of emotion are collateral and concurrent (*ibid.*, pp. 265–267).

41. As we shall note more fully, Sherrington in this passage reveals himself as an advocate of what Franklin Fearing calls the "genetic" view of reflex actions: certain specific characteristics are assigned to reflex actions, but the continuity of the series from reflexes to "willed actions" is emphasized (Fearing, *Reflex Action: A Study in the History of Physiological Psychology,* p. 289). Goltz's and Sherrington's observations on the "bodily resonance of emotion" in decorticate animals can be interpreted in the light of more recent knowledge. Emotion, as they knew, is composed of a subjective or "psychical" experience and an objective physical reaction. The objective reaction may be shown by almost any somatic or visceral organ in the body. As the work of Bard, Cannon, and others has shown, the objective and subjective phases of an animal's emotion can be dissociated by separating the hypothalamus and the cerebral cortex. A decorticate cat with the hypothalamus intact goes into a fit of *sham rage* at the least provocation, but because it is without its telencephalon it probably does not experience subjective emotion. Conversely, emotional reactions are abolished when the hypothalamus is destroyed. On these bases the hypothalamus, which is normally under the influence of the thalamus and cerebrum, is thought to be the integrative center for emotional reactions.

42. By 1906 localization studies had revealed little about the cerebellum's functions, although it was thought to have some role in motor coordination. Today, in accordance with Sherrington's views, three main classes of functions are assigned to the cerebellum: equilibration, postural reflexes, and synergic functions in voluntary movements. The major outlines of the cerebrum's functions were much clearer at the time of the Silliman Lectures. Anatomical and physiological studies had shown: that it is the seat of "mental" functions such as memory, perception, and consciousness; that impulses from sense receptors are brought together into certain fairly circumscribed *sensory areas* of the cerebral cortex; and that neurones discharging impulses to muscles are located within a cortical *motor area* in the precentral convolution.

43. *Quart. J. Exptl. Physiol., 11* (1917), 135–222.

44. A series of eight long papers by these men appeared in the *Philosophical Transactions* between 1884 and 1891. Their contents have been ably summarized in Stephen Paget's *Sir Victor Horsley* (New York: Harcourt Brace, 1920), pp. 95–113.

45. "Observations on the physiology of the cerebral cortex of some of the higher apes," *Proc. Roy. Soc., 69* (1901), 206-209.

46. Fulton papers.

47. Sherrington delivered his paper on Dec. 17, 1901, and it was published eleven days later as "An address on localization in the 'motor' cerebral cortex," *Brit. Med. J., 2* (1901), 1857–1859.

48. Fulton papers.

49. The maps were widely reproduced for many years, and, as Granit

states, "we have not since found it necessary to alter in any fundamental way the picture Leyton and Sherrington gave of the functional organization of the motor cortex even though the number of sites in the cortex from which motor effects can be elicited has increased" (*Charles Scott Sherrington: An Appraisal,* p. 90). Sherrington often cautioned against too facile an acceptance of the maps as indicating fixed or rigid motor points. First, he pointed out, electrical stimulation of anaesthetized tissue may greatly distort normal function. Secondly, he stressed, one should never forget "the unspeakable complexity of the reactions thus rudely symbolized and spatially indicated." Finally, reflecting his dualism, he warned that by the use of stimulation and ablation "little light is given in regard to much that goes on in an organ whose chief function is mentality itself" (*The Integrative Action,* pp. 270–271).

50. For example, reflex limb extension and paw closure are not regularly found as local spinal or cortical reactions — they are elicited only by special stimuli under certain conditions. Reflex limb flexion and jaw opening, in contrast, are easily and regularly elicited from both fields.

51. As Sherrington pointed out in his paper on the proprioceptive system, the labyrinth organ of the cerebellum is part of the system maintaining the tonic postural system. From his study of Sherrington's post-1906 papers, Granit points out that Sherrington eventually identified the tonic system with the extensor muscles counteracting gravity and the phasic system chiefly with the flexor muscles. "Gradually he ceased to emphasize the differentiation as originally formulated" (*Charles Scott Sherrington: An Appraisal,* p. 155).

52. See above, pp. 90–91, 120, 156.

53. The distance receptors (eyes, ears, and nose) are those exteroceptors of the head which have developed especially to "lead" or predominate in the vertebrate's motor taxis. Stimulated by the external matter in direct contact with them, these receptors generate reflex reactions which show adaption to environmental objects at a distance (*The Integratice Action,* pp. 322–324).

54. Conversely, Sherrington observed, once an animal's distance receptors and their reflex reactions are gone, even intense stimuli do not *readily* move or stop the animal as a whole. It is quite hard, for example, to make the spinal frog swim or jump (*The Integrative Action,* pp. 327–328).

55. Compare this statement with Sherrington's Marshall Hall Lecture comment on the effects of spinal transections (see above, pp. 99–100).

56. See Appendix F.

57. In *Reflex Action,* Franklin Fearing distinguishes three "physiological interpretations" of reflex actions current in the first decades of this century: (1) the "specific theory," holding that a reflex is qualitatively different from all other types of animal responses, such as willed, learned, or automatic reactions; (2) the "mechanical group," holding that the characteristics of reflexes are those of all neuromuscular actions; and (3) the "genetic group," assigning certain specific characteristics to reflexes but emphasizing a continuity from reflexes to willed actions (pp. 288–296). Fearing placed Sherrington in the "genetic group," chiefly on the

basis of the latter's statement in Lecture X that "the transition from reflex action to volitional is not abrupt and sharp" (*The Integrative Action,* p. 387). While Sherrington did recognize interactions and transpositions between reflex and volitional actions by an individual, he also maintained a definite separateness between the two types of actions. For as a dualist, a fact which Fearing failed to consider, Sherrington held that volitional activities are "mental events" manifested through but not a product of physical brain. Similarly, as he stated in *Man on His Nature,* Sherrington felt that "recognizable mind" has evolved *with but not from* the nervous system: "The conative motor act, mechanically integrating the individual, would seem to have started mind on its road to recognizability . . . As motor integration proceeds mind proceeds with it . . . But mind seems to come from nothing and to return to nothing" (pp. 197, 267).

58. One significant contribution to the needed new instrumentation was made by Sherrington and his Oxford pupils during the 1920's, when they brought the isometric mirror myograph into customary use. With the isometric method of recording, reflexes could be quantitated and central excitatory and inhibitory processes measured and balanced against each other. Such measurements led, among other results, to Sherrington's definition of occlusion and the subliminal fringe of excitation as types of excitatory and inhibitory processes.

59. Letter, August 13, 1936 (Fulton papers).

60. Sherrington's judgment against a physical monism emerges clearly in two passages from *Man on His Nature.* "The energy concept of Science collects all so-called 'forms' of energy into a flock and looks in vain for mind among them" (p. 266). "Physiology has got so far . . . as examining the activity in the 'mental' part of brain when activity there is in normal progress . . . But has it brought us to the 'mind?' It has brought us to the brain as a telephone exchange" (p. 282). On a philosophic plane, Sherrington was equally unable to accept an idealist monism such as that formulated by Bishop Berkeley (1685–1753), "in which the whole scheme [mind, body, and apprehended world] is a mental one" (*The Integrative Action,* p. xix). For Sherrington the Berkeleian view "would impair the 'zest' of the waking day," nor could he "imagine the achievements of ancient Rome emerging from such a doctrine" (*ibid.,* p. xx).

61. Quoted by Brain in a symposium discussion of a paper by H. W. Magoun, "Early developments of ideas relating the mind to the brain," *Ciba Foundation Symposium on the Neurological Bases of Behaviour, in Commemoration of Sir Charles Scott Sherrington,* ed. G. E. W. Wolstenholme and C. M. O'Connor (Boston: Little, Brown and Co., 1948), p. 24.

CHAPTER VIII: "THE REFLEX WAS A VERY USEFUL IDEA"

1. Fulton, "The historical contribution of physiology to neurophysiology," in *Science, Medicine, and History,* ed. E. A. Underwood, II, 543.

2. Ragnar Granit, *Charles Scott Sherrington: An Appraisal,* pp. 28–29.

3. *Ibid.,* pp. 6, 4.

4. *The Endeavour of Jean Fernel,* p. 142.

5. Granit, *Charles Scott Sherrington: An Appraisal,* p. 26.

6. Thomas Kuhn, *The Structure of Scientific Revolutions* (Chicago: University of Chicago Press, 1962), p. 10.

7. *Ibid.,* pp. 16–17.

8. Denny-Brown, "The Sherrington school of physiology," *J. Neurophysiol., 20* (1957), 543–548.

9. Sherrington and Liddell, "Reflexes in response to stretch *(myotatic* reflexes)," *Proc. Roy. Soc., 86B* (1924), 212–242; Sherrington, "Remarks on some aspects of reflex inhibition," *Proc. Roy. Soc., 97B* (1925), 519–545; Sherrington and Eccles, "Numbers and contraction values of individual motor-units examined in some muscles of the limb," *Proc. Roy. Soc., 106B* (1930), 326–357.

10. Eccles, "The development of ideas on the synapse," in *The Historical Development of Physiological Thought,* ed. Chandler M. Brooks and Paul F. Cranefield, p. 43.

11. History of biology lecture, Harvard University, May 5, 1965 (unpublished).

12. Bernard, *An Introduction to the Study of Experimental Medicine,* trans. H. C. Greene (New York: Collier Books, 1961), p. 69. Published in 1865 as *Introduction à l'étude de la medicine expérimentale.*

13. *Brit. Assoc. Rep.* (1922), pp. 3–4.

14. *Charles Scott Sherrington: An Appraisal,* pp. 37–38.

15. Sherrington did draw some analogies between physical and neural phenomena — such as comparing the brain with a telephone exchange and latency and after-discharge with inertia and momentum.

16. *The Integrative Action,* p. 7; "Comparative neurophysiology," in *Evolution of Nervous Control from Primitive Organisms to Man,"* ed. Allan D. Bass (Washington: American Association for the Advancement of Science, 1959), pp. 33–34; "Evolution of conduction in the nervous system," in *Evolution of Nervous Control,* p. 78.

17. *Charles Scott Sherrington: An Appraisal,* pp. 107–108. Reviewing the 1947 reissue of *The Integrative Action,* F. M. R. Walshe expressed a view paralleling Granit's. "In its new form," Walshe wrote of *The Integrative Action,* "this classic book . . . should invigorate the work and thought of new generations of physiologists . . . in this age of immense technical ingenuity, when it has become difficult to contemplate the facts of observation with the leisure and calm that their philosophical synthesis demands" ("A physiological tribute. *The Integrative Action of the Nervous System," Endeavour, 7* [1948], 39).

18. Many researchers have expressed an awareness of biology's needs for its own conceptual statements. In a paper on "The concepts of integrative levels and biology," for example, Alex B. Novikoff wrote, "No matter how complete our knowledge of the chemistry and physics of living systems becomes in the future, living substance must still be recognized as matter on a higher level, with new, unique properties which have emerged on combination of the lower-level units. When molecules become part of a highly integrated system, protoplasm, it is important to know the properties of molecules, but protoplasmic behavior needs description in

terms and laws which have no meaning for molecules, in specifically biological terms and laws" (*Science, 101* [1945], 211).

APPENDICES

1. *Who Was Who, 1951–1960* (London: Adam and Charles Black, 1961), 994.

2. Sherrington began his work at St. Thomas's Hospital in Sept. 1876.

3. Taken from "Notes on the arrangement of some motor fibres in the lumbo-sacral plexus," *J. Physiol., 13* (1892), 658–661.

4. "Experiments in examination of the peripheral distribution of the fibres of the posterior roots of some spinal nerves (II)," *Philos. Trans., 190B* (1898), 45–49.

5. The following syllabus was supplied by Miss Madeline Stanton, Librarian of Historical Collections, Yale University Historical and Medical Library.

6. R. S. Creed, "Obituary Notice: Sir Charles Scott Sherrington," *Brit. J. Psychol., 44* (1953), 1.

7. *Man on His Nature,* p. 125.

8. These five papers, published in 1896, 1897, 1902, and 1904, are listed in the bibliography. The fourth, and longest, paper, "On binocular flicker and the correlation of activity of 'corresponding' retinal points," appeared in the first volume of the *British Journal of Psychology* (1904). In the judgment of one authority the work which Sherrington reported in this paper "ranks with Wheatstone's first description of stereoscopic vision [1838] as one of the most illuminating experimental studies of the problems of binocular vision" (Creed, *Brit. J. Psychol., 44,* 1).

9. *The Integrative Action of the Nervous System,* pp. 353–354.

10. *Ibid.,* p. 355.

11. *Ibid.,* p. 356.

12. Adrian, "The analysis of the nervous system: Sherrington Memorial Lecture," *Proc. Roy. Soc. Med., 50,* 995. Since the work of Johannes Muller and others in the nineteenth century who elaborated notions put forth since the time of Galen, the singleness of perception in binocular vision has been explained anatomically: (1) the eyes' retinas are composed of corresponding "retino-cerebral points"; (2) an optic nerve originates from each retina and terminates in the cortex of the brain's occipital lobe; (3) after leaving the eye *one-half* of the fibers from each retina cross at the optic chiasma: thus, the right optic tract reaches the occipital lobe carrying fibers from *both* the left and right retinas; (4) the projections of the retinas on the brain via their nerve fibers are superimposed on the visual cortex, and singleness of vision results when one brain pattern coincides point for point with the other. (For a detailed study of the history of work on the psychophysiology of vision see E. G. Boring, *Sensation and Perception in the History of Experimental Psychology* [N.Y.: Appleton-Century-Crofts, 1942].)

13. *The Integrative Action,* p. 382. Sherrington's view of the optic paths' function was one basis for the following "apologia" in his 1932 Rede Lecture on "The brain and its mechanism": "I may seem to stress

the preoccupation of the brain with muscle. Can we stress too much the preoccupation when any path we trace in the brain leads directly or indirectly to muscle?" (Cambridge: Cambridge University Press, p. 10).

14. *The Integrative Action,* pp. 377, 380.

15. *Ibid.,* p. 381; *Man on His Nature,* p. 273.

16. For a recent assessment of binocular vision and flicker-fusion studies see H. S. Bartley, "Central mechanisms of vision," *Handbook of Physiology.* Section 1., chap. xxx; *The Integrative Action,* p. 381.

17. *The Integrative Action,* p. 381.

18. *Ibid.,* pp. 385, 386; "pure reflexes," Sherrington stated, are those "devoid of psychical accompaniment so far as introspection can discover" (*ibid.*).

19. *Ibid.,* pp. 385, 390.

20. December 10, 1925 (Fulton papers).

21. Fulton papers.

22. The Cambridge University Press has no records of Sherrington's psychology textbook (letter from A. K. Parker, assistant secretary, Cambridge University Press, to the author, December 11, 1964). When I wrote to Carr Sherrington, quoting Fulton's two statements, he replied: "This is all news to me and is *most* surprising. To my knowledge he never even conceived the thought of a book on 'Psychology.' He would have considered it impinging on the work of C. S. Myers and William McDougall. There is no trace in any correspondence of any reference to such a thought. There is some misunderstanding here" (to the author, December 28, 1964).

23. *The Integrative Action,* Foreword to 1947 edition, p. xv.

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The literature which I have consulted in the course of studying Sherrington's work is divided into four categories: unpublished material; works by Charles Sherrington, arranged in chronological order; primary sources; secondary sources.

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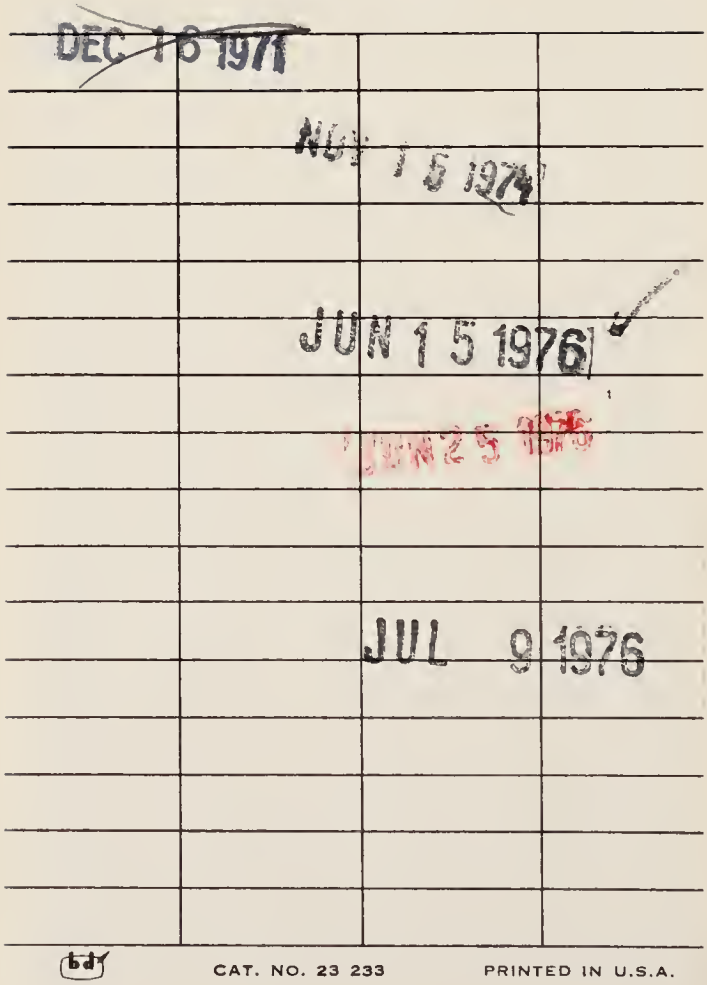

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